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Original Communications

LOWER ESOPHAGEAL WEB

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(BY INVITATION)
SYRACUSE, N. Y.

IN THE past when a patient presented himself to the physician, his chief complaint being difficulty in swallowing, diagnostic techniques were primarily focused on confirming or ruling out the presence of carcinoma, impacted foreign body, diverticula, stricture or cardiospasm, etc. Failure to demonstrate pathology of the pharynx, esophagus, or stomach, left the conscientious physician with the logical assumption that the complaints of the patient were on a functional rather than organic basis.

In 1953, Ingelfinger and Kramer[1] published an article in which they discussed 6 patients each of whom was suffering from dysphagia. Endoscopic examinations of these patients were negative but these authors described roentgenologic observations which they referred to as a "contractile esophageal ring." The same year Schatzki and Gary[2] reported similar x-ray findings on 5 of their patients and interpreted them with the term "lower esophageal ring." The true nature of the lesion was at first not clear to these men. But their original work, their subsequent investigation, and our own experience lead us to believe that many of these patients who have had categorical diagnoses of "functional dysphagia" have, in fact, cases of an organic narrowing of the lower esophageal lumen. This so-called "ring" or "web" is responsible for the symptoms of the patient and these same symptoms disappear once the condition is corrected by surgery.

CLINICAL PICTURE

The type and degree of dysphagia conform to and are consistent with the nature of the lesion. The onset may or may not be acute. It is apparently determined by the relative obstructive potential of the food ingested. For

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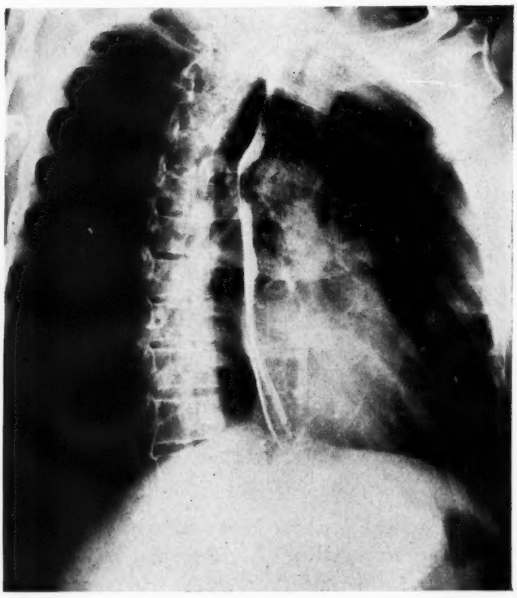

Fig. 1.—Case 1. Thin barium used. Normal-appearing esophagus on first admission.

Fig. 2.—Case 1. Thick barium swallow, first admission. Reveals web, but not diagnosed as such.

example, an abrupt change in eating habits from the ingestion of soft food to the ingestion of heavy solids or a poorly masticated bolus may readily produce an acute obstructive episode. Conversely, if the eating habits of the same individual remain unchanged, the onset of dysphagia most likely will be insidious. In either event, once dysphagia has become established, the course is likely to be protracted, of an episodal nature, and may finally become incapacitating.

During the early stages, dysphagia in our cases seemed to have been related to the obstructive potential of the bolus swallowed. Meat and bread were most likely to produce symptoms. Obstruction was associated with low substernal discomfort and a sensation of something being stuck in the lower chest. Drinking water would often alleviate symptoms. For years by careful mastication and scrupulously restricting the diet, severe symptoms were curbed. However, in our cases, dysphagia finally became so severe that intake had consisted essentially of a liquid diet for the year prior to surgery. Neither

Fig. 3.—Case 1. Thick barium. Second admission six months later. Web not diagnosed but operation advised for obstructing lesion.

patient had experienced vomiting, nausea, or heartburn. Both had traveled from one physician to another seeking relief. They were subjected to repeated endoscopic examinations and barium swallows, but such efforts failed to establish a diagnosis. Consequently, the impressive histories and negative findings had led to the frequently mistaken diagnosis of neurosis.

ROENTGEN FINDINGS

Figs. 1 and 2 are x-ray pictures showing a barium swallow in the first patient (H. T.) who was experiencing severe dysphagia at the time. It was

Fig. 4.—Case 2. Thin barium. Interpreted as normal. Marked symptoms at time of examination.

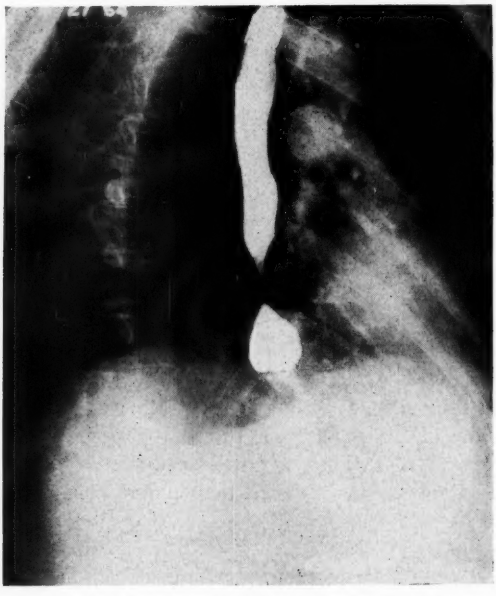

Fig. 5.—Case 2. Thick barium. Second admission, two years later. Web diagnosed.

reported as within normal limits by the consensus of observers, although one man felt sure it represented a stricture. Fig. 3 is a repeat x-ray photograph of the same patient a few months later. A definite weblike structure was demonstrated 5 cm. above the diaphragm and proximal to the esophagogastric junction. Of significance is the fact that the web was not demonstrable until the esophagus above and below it was distended with thick barium. This technique allowed the lumen of the esophagus above and below to exceed the diameter of the lumen of the web.

Fig. 6.—Case 2. Spot film of web.

Fig. 4 shows an x-ray of a barium swallow in Case 2. Again the original interpretation was that there was no esophageal pathology. Figs. 5 and 6 are x-rays of the esophagus of the same patient two years later. The barium-filled esophagus demonstrates very clearly the weblike structure. Schatzki and Gary clearly describe this lesion in the 5 cases reported in 1953 as a "lower esophageal ring." Their report describes typical x-ray findings although in a subsequent report they were frank to say, "The nature of the abnormality and its origin are not known, but the clinical and roentgenological pictures are characteristic." Our roentgenologic findings demonstrate a thin "web" in the lower esophagus, located 3 to 5 cm. proximal to the esophagogastric junction. It is constant in location and is demonstrable only

when the esophagus above and below is distended sufficiently to exceed the diameter of the web. When the esophagus is collapsed the lesion is likely to be missed.

The web is smooth, varying in thickness from 3 to 5 mm. and produces a constant narrowing located centrally, thus producing a "shelflike" symmetrical shadow on the roentgenograms. The lumen in one patient was 3 mm.; it was 5 mm. in the other. The esophagus above the narrowing characteristically is not widened and proximally peristalsis functions normally.

ESOPHAGOSCOPIC FINDINGS

Case 1 had three esophagoscopies performed elsewhere in 1953, each reported as normal. Preoperative esophagoscopy by us in 1954 was reported as essentially normal but the operator experienced difficulty in passing the area interpreted as cardia. The mucosa appeared normal.

Similarly, esophagoscopy of the second patient performed by us in 1952 was recorded as being normal. The instrument was passed into the stomach without difficulty. A second esophagoscopy on this patient was not performed later because repeat roentgenograms were diagnostic of a web.

It is interesting to note that Ingelfinger and Kramer's experience[1] as well as Schatzki and Gary's[2] parallels ours, relative to endoscopic failure. Three of Ingelfinger and Kramer's patients were esophagoscoped and no lesion demonstrated. Four of Schatzki and Gary's were esophagoscoped. The lesion was seen in only one instance.

OPERATIVE AND PATHOLOGIC FINDINGS

At thoracotomy the lesion can easily be demonstrated by opening the esophagus longitudinally a few centimeters proximal to the contemplated site of obstruction and inserting a finger into the esophagus. Once the web has been identified, it is intussuscepted upward by the index finger inserted through a gastrotomy incision (Fig. 8). By internal palpation and this maneuver, the lesion can be easily demonstrated and clearly visualized; with external esophageal palpation the lesion may not be felt. In one case the defect could not be felt externally although a ringlike thickening deep in the wall of the esophagus was palpated.

With a finger in the esophagus, a definite impression was gained that this was a weblike projection into the lumen. The web was leathery in consistency and pliable. The small lumen in both cases (3 to 5 mm., respectively) could barely be felt with the finger tip.

The mucosa above and below the defect felt normal. The obstruction was located above the esophagogastric junction, there being 3 to 5 cm. of normal-appearing esophagus seen below the level of obstruction. In Case 2 a ringlike thickening was present at the base of the web in the esophageal wall.

The elected operative procedure was simple, designed primarily to preserve the integrity of the esophagogastric junction, to alleviate obstruction, and to avoid subsequent stenosis and fibrosis at the operative site. The technique employed is illustrated in Figs. 7, 8, 9, and 10. After the lesion was

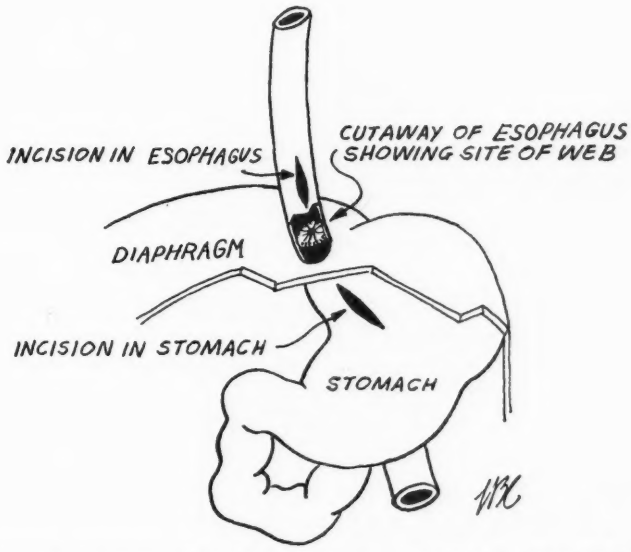

Fig. 7.—Schematic illustration of web in situ with incisions made in esophagus and stomach.

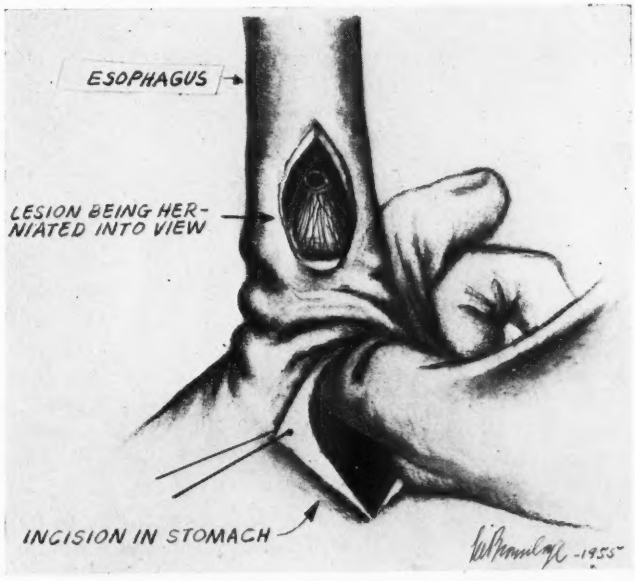

Fig. 8.—Artist's conception of web being intussuscepted upward with left index finger in stomach.

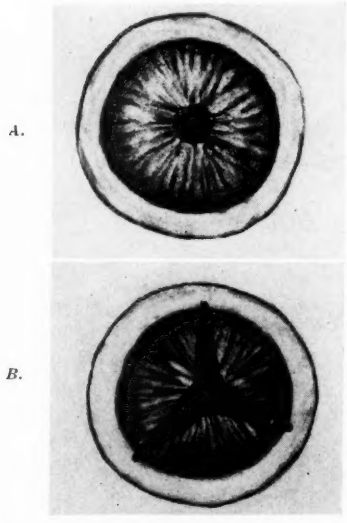

Fig. 9.—Drawing of web and wedges resected. *A*, Cross section of esophagus from above showing weblike membrane. *B*, Cross section of esophagus from above showing wedge-shaped pieces removed from membrane.

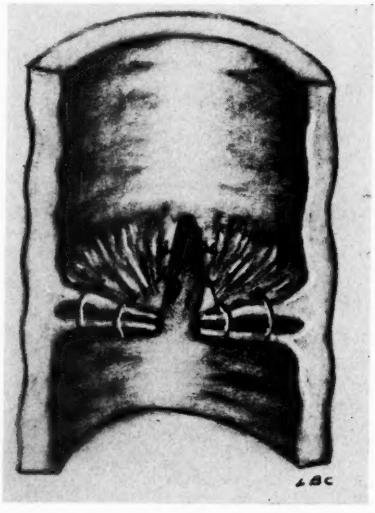

Fig. 10.—Longitudinal section of esophagus showing sutured flaps of weblike membrane. Drawing of repair after wedge resection.

exposed, three pie-shaped wedges of the membrane were removed leaving intervening areas of mucosa at the base to prevent subsequent stricture. The raw areas were sutured with interrupted silk sutures and the stomach and esophagus closed. A Levine tube was then passed into the stomach and the chest closed.

Liquids were started orally on the third postoperative day and solids were given before the seventh postoperative day. To date, the patients are totally relieved of dysphagia, being completely asymptomatic at the seventh and eighth postoperative months, respectively.

PATHOLOGY

At surgery the lesion in each case presented a definite membranous appearance. The esophageal lumina were small, measuring 3 to 5 mm., and were centrally located. The surfaces were smooth having the appearance of normal esophageal mucosa. In each, the web was pliable and felt not unlike the leathery type of a stenosed mitral valve.

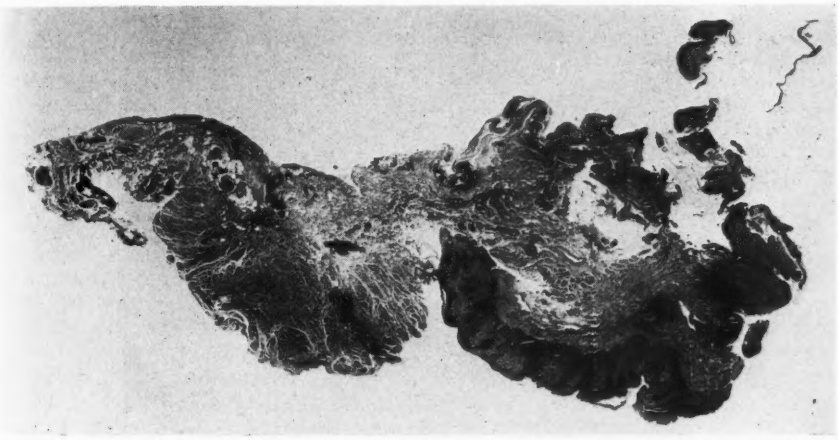

Fig. 11.—Photomicrograph of section of piece of web resected.

Microscopically, the histologic features seen in the wedgelike resected segment were most informative (Figs. 11 and 12). One figure gave a fair indication of the radius of the web although it had decreased in size from fixation. It measured 10 mm. in the fixed state. Squamous-cell epithelium could be seen covering the upper and lower surfaces of the web. There was considerable squamous-cell hyperplasia with folding and piling up of surface epithelium. In many areas associated parakeratosis could be seen. The section clearly demonstrated that mucosa covers the entire surface of the web, although, in one area of this section, a denuded area was seen. The submucosa showed considerable chronic inflammatory cellular infiltration most prominent at the luminal surface where one would expect the most trauma. The outer layer consisted of smooth

muscle. At the junction of the web and esophageal wall, smooth muscle could be seen. This abrupt cessation of the mucosa corresponded to the apex of the wedge located in the muscular wall of the esophagus.

The one case reported by Schatzki in which operation was performed revealed similar marked hyperkeratosis and no evidence of ulcer scar or inflammation. Ingelfinger and Kramer's case that was operated upon revealed only thickened muscular wall.

Fig. 12.—Photomicrograph of web biopsy showing hyperkeratosis, inflammation, and circular muscle.

DIFFERENTIAL DIAGNOSIS

The roentgenologic diagnosis of this lesion should not be difficult. It may be deceiving but if the proper diagnostic maneuvers are made, it is less so. The incidence of diagnosis is probably directly proportional to the observer's index of suspicion. With a thin barium swallow, a web may be easily missed. Even when a high degree of obstruction is present, there is very little hesitation of thin barium in passing through the esophagus. A satisfactory examination requires the ingestion of thick barium, in an amount sufficient to fill and thus dilate the esophagus proximal and distal to the web.

The lesion most likely to be confused with a lower esophageal web is an esophageal stricture. Both lesions do not dilate beyond a certain diameter

and both may be located in the same area of the esophagus. There are several differential points. A web is symmetrical both circumferentially and longitudinally; the converse is likely to be the case with stricture. The narrowed area relative to a web is likely to be short and thin whereas a strictured area usually is longer and thicker. Further differential points are the lack of delayed emptying and negative endoscopic findings in the instance of the web.

Cancer can be quickly eliminated because of the smoothness and thinness of the mucosa and the aforementioned reasons relative to a web. There is no similarity to achalasia. Dilatation proximally, as well as abnormal peristalsis and delayed emptying, is characteristically absent.

CASE REPORTS

CASE 1.—H. T., a 55-year-old man, whose first admission to Syracuse University Hospital was on Dec. 22, 1953, with the chief complaint of intermittent dysphagia of four years' duration.

Present Illness.—He stated that approximately four years before he began having recurrent mild attacks of having certain foods "stick" in the lower chest. Foods most likely to provoke an attack were beef, scalloped potatoes, corn, and bread. For two years, symptoms were alleviated by the ingestion of fluids whenever something became "caught." During the third year of his difficulty he controlled symptoms by chewing foods very well and "abstaining from those most likely to cause trouble." Symptoms during the year prior to admission were characterized by more severe obstruction. Many times liquids would fail to relieve symptoms. Occasionally, induced vomiting was necessary. For about a year his diet had been restricted, by his own volition, to ice cream, milk, and cereal. Heart burn, radiating pain, and nausea were absent. There was no weight loss.

After three years of dysphagia, he sought medical advice. Three esophagoscopies and barium studies were done elsewhere. After each examination he was told that he had a "nervous condition." When the situation became desperate, he was transferred to us for evaluation.

Physical examination revealed a well-developed, well-nourished man who was cooperative, intelligent, and did not appear ill. Physical findings were essentially normal.

Esophagoscopy on Dec. 23, 1953, was not remarkable except that at the cardia (50 cm.), resistance was encountered. The endoscopist interpreted this as the cardia. A biopsy of the mucosa in this area was performed although it appeared to be perfectly normal. It was reported as normal mucosal epithelium.

An investigation of the upper gastrointestinal tract by barium roentgenograms was performed. Several roentgenologists agreed that no definite abnormality could be demonstrated. One observer noted a small area of narrowing several centimeters above the cardia. The consensus believed this to be a peristaltic wave, although one observer believed it to be a stricture.

The patient was discharged on Dec. 24, 1953, with a tentative diagnosis of dysphagia of functional origin and with the recommendation that he return for a recheck examination in one month. He returned to his home in northern New York State and was not heard from until July, 1954.

The family physician informed us that the patient's condition had become so severe that the intake of only liquids had recently become ineffectual.

This sequence of events "spelled out" cancer to the patient. His wife informed the family doctor that her husband had begun to utter suicidal threats. He was then returned to us for further investigation. He was readmitted to University Hospital on Aug. 1, 1954. Examination was unchanged from that of the previous admission except for a 5 pound weight loss and an extreme anxiety state.

A repeat barium swallow with a thick mixture revealed a distinct narrowing 5 cm. proximal to the cardia (Fig. 3). Surgery was advised because of the obstructive symptoms although "web" was not diagnosed. Esophagoscopy was not repeated.

On Aug. 2, 1954, at thoracotomy, no abnormality could be visualized or palpated until the esophagus had been opened. A 3 cm. longitudinal incision was made proximal to the predetermined site of obstruction. When a finger was inserted into the lumen, a definite obstruction was palpated approximately 3 cm. above the cardia. To obtain accurate visualization and mobilization of this defect, it was decided to open the diaphragm and to make a counter gastrotomy incision. With a finger in the stomach, the lesion was then herniated or intussuscepted into the esophageal incision. Excellent control and exposure were obtained (Figs. 7, 8, and 9).

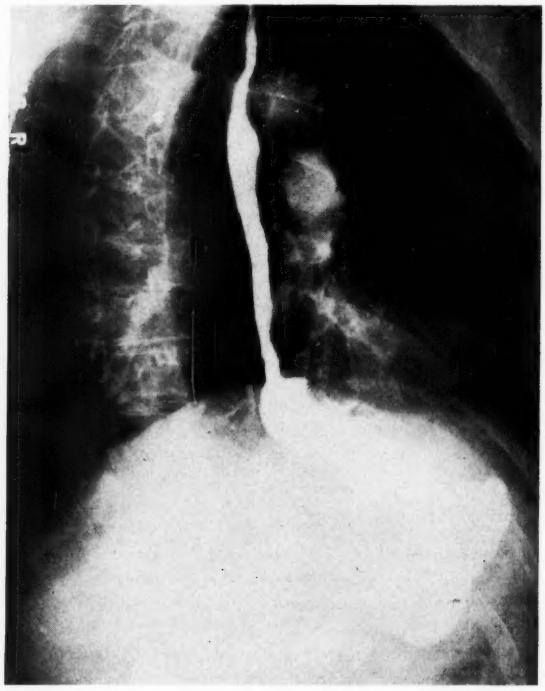

Fig. 13.—Postoperative esophagograms of Case 1.

The obstruction was a definite weblike structure having the characteristics described. A plastic procedure previously described in detail was performed (Figs. 9 and 10).

The postoperative course was uneventful. Postoperative roentgenograms are shown (Fig. 13). The patient has been completely relieved of dysphagia and is absolutely free of symptoms. He has returned to a normal diet.

CASE 2.—W. M., a man 55 years of age, entered Syracuse University Hospital on Sept. 12, 1954, with the chief complaint of intermittent dysphagia of seven years' duration.

Present Illness.—The patient stated that 15 years before during an ethanol bout at Thanksgiving, "I almost choked to death after swallowing a large piece of gizzard." He didn't recall further trouble until 1947 when he noted the slow onset of intermittent dysphagia. He recalled having difficulty swallowing large pieces of beef steak and similar large pieces of meat. He noted a sensation of "having a lump in my lower chest," usually relieved by

swallowing some liquid. After a year or so, he noted that his eating habits had changed. Chewing food more thoroughly became routine. Strict adherence to this regimen relieved symptoms for several years.

During the two years prior to admission, strict eating habits no longer were effective. For two years his diet was of necessity restricted to liquids, ice cream, and fine cereals.

He was esophagoscoped by us in 1952 but no lesion was found. The stomach was readily entered. Barium studies revealed a normally emptying esophagus (Fig. 4). He was, therefore, told that he had a "nervous condition" and was given pills. He then found that pills would often cause severe symptoms. He denied heartburn, pain, vomiting, and weight loss. He was re-evaluated by us in September, 1954.

Physical examination was essentially negative. The patient was a well-developed, well-nourished businessman. He did not appear acutely or chronically ill.

Esophagoscopy was not repeated. Barium study of the esophagus revealed a typical web located just proximal to the cardia. The lumen measured 3 mm. (Figs. 5 and 6).

Fig. 14.—Postoperative esophagograms of Case 2.

At exploratory thoracotomy on Sept. 13, 1954, the findings and operative procedure as described in Case 1 were almost identical except that the lesion was palpable before the esophagus was opened. It presented as a firm localized circumferential thickening in the esophageal wall. This area corresponded to the base of the web.

The described plastic repair was performed.

The postoperative roentgenogram is shown in Fig. 14.

The patient has been completely relieved of dysphagia and when seen in March, 1955 (6 months postoperatively), he stated, "It's like living anew. I can eat everything now."

COMMENT AND DISCUSSION

Ingelfinger and Kramer deserve credit for first reporting the salient roentgenographic findings of this lesion, although they were not certain of

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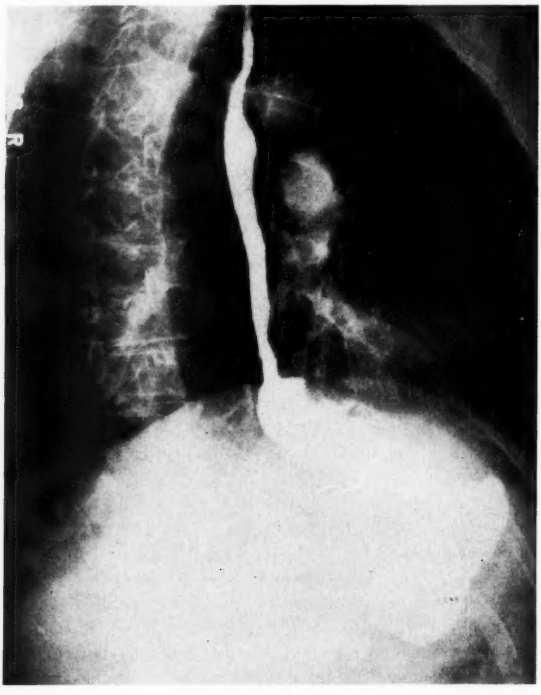

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the exact nature of the structure they were describing. They called it a "contractile esophageal ring" and, although 1 case was treated with resection and esophagogastric anastomosis, the pathology of the lesion was not determined.

Schatzki and Gary described accurately the x-ray findings of this lesion and called it a "lower esophageal ring." Although one of their patients was operated on and had an esophagoplasty, they, too, were uncertain about the exact nature of the lesion. We believe that Schatzki and Gary were precise in their original comments and description of this entity as a fixed "ring" which is present at all times although visible only when the esophagus proximal and distal to it is distended more than the maximal diameter of the "ring." Ingelfinger and Kramer believed that the lesion was not preformed, that it occurred as a peristaltic wave approached the lower esophagus, and that the ring might have migrated down the esophagus toward the diaphragm. We are in agreement with Schatzki and Gary's original report and in disagreement with Ingelfinger and Kramer regarding these x-ray findings. However, in a subsequent report, one year later, Schatzki and Gary were inclined to believe that the ring represented the herniated esophagogastric junction. They regarded the narrowing as caused, not by an abnormal muscular contraction, but by an inability of the esophagogastric junction to distend beyond a certain diameter. They stated, "The nature of the abnormality and its origin are not known, but the clinical and roentgenologic pictures are characteristic."[3]

Surgery in our 2 cases has proved the actual identity of the lesion to be a firm, moderately rigid web (or diaphragm) comprised of hyperplastic squamous-cell epithelium, submucosa, and muscularis quite similar to the normal lower esophageal wall. The web is about 3 mm. thick. In the first case the lumen was 3 mm. in diameter, in the second it was 5 mm. It is intraesophageal, about 3 cm. above the esophagogastric junction. In the second case, in addition to the web, there was a thickened intramural ring within the muscular wall the nature of which is not known. Both cases were undiagnosed with the first barium x-ray studies. Both were undiagnosed at esophagoscopy. This may seem faulty and difficult to understand. In each instance the instrument was passed to the obstruction, but it was not visualized as such. The endoscopist thought it was merely a matter of a difficult cardia to pass, since there was no tumor, ulcer, esophagitis, or visible stricture.* Both cases were operated upon in light of the subsequent x-ray findings, plus the severe obstructive symptoms. In the first case, the esophagus appeared normal and was negative to palpation. An esophagotomy was done about 4 cm. above the cardia and the obstruction palpated. The end of a Kelly clamp could be passed through the lumen. With the left index finger introduced through a gastrotomy incision, the web was forced upward into the esophagotomy and a local plastic operation was done. In this manner, the cardia was preserved. In the second

*With our present knowledge and experience, we think endoscopy will be properly interpreted in future cases of web.

case, the web was treated in the identical manner. The coexisting "ring" was incised and fractured. In this case, the ring was palpated externally. Clinically, this simple plastic procedure has proved to be completely effective.

Why does symptomatology occur late in life when the lesion is apparently congenital in origin? This poses an interesting problem and may stimulate considerable speculation. Is there sufficient hyperplasia of the mucosal epithelium and resultant "folding" of the layer to account for a change in lumen size? Does trauma, with associated edema and chronic inflammatory reaction, influence the mobility of the web? Perhaps these changes explain the mechanism of late symptoms. Currently, there are insufficient data to make positive statements regarding these questions. It is hoped that subsequent investigation will supply the answer.

SUMMARY AND CONCLUSIONS

1. Two case reports have been reviewed illustrating a generally unrecognized clinical entity which causes dysphagia.
2. The etiological factor has been clearly established as a membranous weblike structure occurring in the lower third of the esophagus.
3. Its pathologic and clinical characteristics have been discussed.
4. A successful operative approach has been described.
5. Lower esophageal web should be included in the differential diagnosis of dysphagia.

We wish to acknowledge the advisory and technical assistance of Dr. Paul Bunn, Associate Professor of Medicine; Dr. Richard B. Jamieson, Assistant Professor of Bacteriology; and Miss Stella Zimmer, Photography Department, State of New York, Upstate Medical Center, Syracuse, New York.

REFERENCES

1. Ingelfinger, F. J., and Kramer, P.: Dysphagia Produced by a Contractile Ring in the Lower Esophagus, Gastroenterology **23**: 419-430, 1953.
2. Schatzki, R., and Gary, J. E.: Dysphagia Due to a Diaphragmlike Localized Narrowing in the Lower Esophagus ("Lower Esophageal Ring"), Am. J. Roentgenol. **70**: 911-922, 1953.
3. Gary, J. E., and Schatzki, R.: Radiologic Examination of the Gastrointestinal Tract, New England J. Med. **251**: 1052-1058, 1954.

DISCUSSION

DR. RICHARD H. SWEET, Boston, Mass.—Dr. Bugden has brought to our attention a most interesting lesion, but I submit that he is confusing two different conditions, because I do not believe that the so-called contraction ring described by Ingelfinger and also by Schatzki is necessarily the same thing. We at Massachusetts General Hospital have been puzzled to explain their findings. I have encountered three actual lower esophageal webs; two in infants and one in an adult, all three operated upon by local procedures such as described by Dr. Bugden and, incidentally, I favor opening the esophagus and doing a circumferential excision of the web.

In the cases that Dr. Schatzki shows us and in Dr. Ingelfinger's cases, one cannot see anything in the esophagus by esophagoscope. The instrument can be passed right into the stomach. On the other hand, these webs, including the three webs I have had, are readily seen by the esophagoscope. In the infants, attempts to dilate them were unsuccessful. There was an obvious mechanical difficulty. Some of the cases that Schatzki calls contrac-

tion rings, I believe are small hiatus hernias where the esophagogastric junction is a little above the diaphragm, and not infrequently these patients with almost unrecognizable small hiatus hernias may have obstruction when they change their feeding habits, as Dr. Bugden has pointed out. But I think he is talking about two entirely different conditions here today.

DR. RALPH ADAMS, Boston, Mass.—Almost everybody in this Association has a case of almost anything, and I do not want to duplicate the lung abscess experience of a few years ago when practically every youngster present seemed to have one to report. But in the two cases of web of the type pictured, I think that the treatment may be much simpler than that diagramed and exemplified. I am sure there are two different conditions; Dr. Sweet brought that out. They may be distinguished by careful fluoroscopic and x-ray examination. No esophagus has been properly examined until the patient has been fluoroscoped in the Trendelenburg position. If bread is mixed with barium, thin barium becomes the functional equivalent of thick barium. In the Trendelenburg position, if one gives thin barium and then a swallow of thick barium subsequently, lower esophageal lesions, and particularly this one, are made evident more easily and more beautifully than by any other method. Dilatation by means of inflatable bag bouginage will correct these affairs very promptly and in a minimum length of time.

DR. MAX G. CARTER, New Haven, Conn.—I am tremendously interested in this problem and delighted to see that it is again brought to light by Dr. Bugden, but I rather agree with Dr. Sweet that perhaps he may have a different concept of what Dr. Schatzki has brought out from what I have. Since our roentgenologist became aware of this disorder some two years ago we have now seen 4 cases. These cases can be identified from the history, at least to some extent, and when they are examined properly with dilatation of the esophagus during fluoroscopy, the diagnosis becomes clear. In not one of these cases was there any abnormality by esophagoscopy except that the esophagoscope entered the stomach somewhat more readily than is usual. We therefore had the feeling that the patients probably had a "short esophagus" type hiatus hernia. This has been confirmed by x-ray. Finally, these patients have been subjected to dilatation by the Hurst mercury bougies which pass easily through a No. 48 F. without the slightest feeling of resistance. I may be in error, but I cannot imagine that would happen so easily with the cases Dr. Bugden showed us.

(Slide) I am sure many of you have seen this illustration from the textbook by Dr. Templeton. He pointed out that this was a lesion which could be identified when the esophagus was distended, was not malignant, and should not be mistaken for malignancy. That was in 1944. Dr. Templeton did not name the lesion.

(Slide) This illustrates a classical "contraction ring." On the right there is distention of the esophagus with air, almost like a contrast enema, showing the narrowed portion.

(Slide) These pictures are of another patient with similar findings. There is the ordinary esophagram on the left and on the right the esophagus when the patient has swallowed bread together with thin barium. Our roentgenologist has become astute in finding these and I would like to ask Dr. Bugden whether he feels that this sort of lesion should be operated on. We have not operated on any of them. The patients report symptoms occurring during periods of emotional stress, when they perhaps eat a little too fast. One patient would get upset when his teen-age son would take the car and keep it out too late; then for a couple of days he would not be able to eat steak. When he learned what his problem was and that when he was angry with his son he had to chew a little more thoroughly, he could eat normally again.

DR. I. DARIN PUPPEL, Columbus, Ohio.—In our experience, the use of a No. 00 barium-filled capsule has been more positive than the use of barium bread in bringing out defects in the lower esophagus.

DR. B. H. RAMSAY, Los Angeles, Calif.—I should like to report the case of a 61-year-old man who was about to commit suicide. He stated that he had had no difficulty whatsoever with swallowing until eight years before, when suddenly, with a normal meal, he

choked and thereafter he had never had anything but barley water and unsweetened gelatine. The correct diagnosis of web obstruction was not made. I operated upon him and did an esophagotomy of the lower 3 inches of esophagus with a Levine tube in place. The esophagus was hypertrophied; the mucosa appeared normal. I asked the anesthetist to pass a Levine tube to the stomach, and it passed the area of narrowing into the proximal inch of the stomach, but no further. In order to investigate this, I inserted my finger into the stomach through a gastrotomy opening and felt a membrane between the finger and the tube. I want to point this out, because this man had had dilations on several occasions by very competent men and each time was told that the esophagus was "like a sponge." Actually, the Levine tube had invaginated a membrane downward into the stomach. There was a dense membrane about 0.5 mm. in thickness with a very small opening in the center. Because these membranes can be displaced or stretched downward, esophageal dilatation may not be simple. If the dilator does not penetrate the opening in the esophageal web, but displaces it downward, the dilatation force is directed against the esophageal wall but cannot affect the web itself.

DR. C. F. STOREY, Portsmouth, Va.—I have had one patient with a lower esophageal web identical to those described by Dr. Bugden except that it was located somewhat higher in the esophagus, near the junction of the lower and middle thirds. This lesion was encountered in a 9-month-old white girl baby who had had increasing dysphagia and regurgitation since birth. She did fairly well on liquid nourishment but was unable to take any type of solid food. At operation through the right chest, the lesion could not be felt through the wall of the mobilized esophagus although it had been accurately localized by preoperative barium swallows. A No. 16 red rubber urethral catheter was passed down the esophagus until the obstruction was met. A 1.5 cm. segment of the esophagus was then resected including, of course, the esophageal web, and esophageal continuity was restored by a two-layer end-to-end anastomosis. Examination of the resected specimen clearly showed that an operation of unnecessary magnitude had been performed. A small longitudinal incision in the muscle coats of the esophagus, resection of the web, and closure as described by Dr. Bugden would have been perfectly adequate. The patient's postoperative course was entirely uncomplicated and there has been no tendency to narrowing at the site of the anastomosis in the eight months that have elapsed since her operation. The child is now able to eat all foods without difficulty.

DR. RALPH BERG, JR., Spokane, Wash.—I would like to make the following remarks in discussing the paper by Dr. Walter F. Bugden and Dr. J. Ernest Delmonico. Since this lesion is uncommon, I wish to present 2 cases diagnosed in childhood.

Slide 1 demonstrates a diaphragmatic obstruction in the distal fourth of the esophagus partially obstructing it. This boy was 23 months old. This second slide demonstrates the findings two weeks following surgical excision of the diaphragm. This is the site of the esophagotomy which you note is the widest portion of the esophagus. Slide 3 shows a radiolucent foreign body obstructing the esophagus by occluding the tiny lumen in a fibrous diaphragm; also in the distal fourth of the esophagus. This child was an 11-month-old girl.

Both patients have obtained complete relief after surgical excision of the diaphragms. Both patients had apparently normal esophageal function until they began to take solid food; then intermittent dysphagia appeared with solids. The boy's lesion was missed in two preceding esophagrams. The family had consulted a host of doctors trying to find the cause of his intermittent dysphagia and they were misled by "negative" radiographic studies.

The first child is about two years postoperative, and the second, one year postoperative. Neither patient has had dysphagia or obstruction since operation and their diets are entirely normal. In both of these patients, the lesion was readily seen at esophagoscopy and attempts at dilatation were failures. Neither of these children had a history of ingestion of corrosive agents.

Although these radiographs seem to be almost identical to those shown by Drs. Bugden and Delmonico, it seems inconceivable that a lesion such as demonstrated here could remain asymptomatic until adult life. Lesions of this type certainly merit further attention.

DR. ERNEST DELMONICO (Closing).—I wish to thank the discussants.

One purpose in presenting this subject was to stimulate interest, discussion, and investigation. From the comments of the previous discussants, I believe the purpose has been fulfilled. With regard to some of the questions raised, we have reserved some ammunition.

(Slide) A third-year medical student came to us one Sunday afternoon with a foreign body lodged in the lower esophagus. Prior to esophagoscopy he related that for several years he was in the habit of carefully masticating his food to avoid dysphagia. Esophagoscopy located a small bolus of meat lodged near the cardia. Following its removal a definite narrowing was visualized near the esophagogastric junction. An attempt to pass the esophagoscope through this area resulted in fracturing the "web" as represented on this postesophagoscopic barium swallow. The patient no longer has dysphagia. This suggests that in some instances the lesion may be treated by endoscopic means.

(Slide) The next patient was a man 55 years of age who complained of having dysphagia for 16 years. The web in this instance was responsible for only mild dysphagia and therefore a corrective procedure was not performed. This slide again illustrates failure of a thin barium swallow to demonstrate the lesion.

(Slide) This is the same case. However, at this time a barium swallow with a bolus of bread was employed. Notice the relatively large diameter of the lumen of this web. Considerable mobility of the web was observed fluoroscopically, which may be a factor in producing only mild obstruction.

Regarding treatment, we are not certain which cases should be treated by the endoscopic route and which by esophagoplasty. There are many variations of webs with regard to size of lumen thickness, pliability, etc. We do feel that the 2 cases reported in our paper could not possibly have been successfully treated endoscopically.

LYMPHOMA OF THE LUNG AND PLEURA

WILLARD VAN HAZEL, M.D.,* AND ROBERT J. JENSIK, M.D.** (BY INVITATION)
CHICAGO, ILL.

THE related lymphogenous diseases, lymphosarcoma and Hodgkin's disease, when occurring in the thorax have usually been considered to be mediastinal lesions. Pulmonary and/or pleural involvement are seen in these disorders in incidence varying up to 33 per cent (parenchymal) and 50 per cent (pleural) (Rubin[1]) but these localizations usually accompany the widespread dissemination seen in advanced, preterminal, or autopsy material.

In Robbin's[2] analysis of a large series of proved lymphoma cases, approximately 7 per cent were considered to have developed a lymphomatous process in the lungs. This analysis eliminated all pleural fluid cases and conceivably excluded some other cases, which possibly accounts for this low figure.

Isolated organ lymphoma has been reported in bowel and stomach and examples of localized lesions, which would have permitted surgical excisions, were seen in 10 per cent of the autopsy material comprising Gall and Mallory's[3] series of proved lymphomas.

More recently, case reports of pulmonary lymphoma treated by lobectomy or pneumonectomy have appeared, the first of these by Churchill,[4] Spatt, and Grayzel,[5] and Maier (1948),[6] although the resection in the latter report actually was done in 1944.

The patient reported upon by Dr. Churchill was again included in Robbins' series, five and one-half years following resection, at which time a recurrence had developed in the lower lobe and in the left lung.

Subsequent reports have also been published by Anlyan, Lovingood, and Klassen (1950)[7]; Beck and Reganis (1951)[8]; Weissman and Christie (1951)[9]; Sarokhan and Morrison (1953)[10]; and Grimes, Weirich, and Stephens (1954).[11]

Our series consists of 12 cases seen from 1945 to the present time at St. Luke's Hospital and Research and Educational Hospital of the University of Illinois and is divided into seven parenchymal and five pleural types. Brief abstracts of these cases follow although a summary of the data appears in Tables I and II.

CASE REPORTS

CASE 1.—January, 1946. The patient (M. W.) was a 27-year-old white woman who had complained of shortness of breath, a cough, and expectoration of whitish sputum for six months. The onset was acute with pain in the left chest and the symptoms had increased in severity until the time of admission with the additional complaints of sweating, weight loss (25 pounds), and weakness.

From St. Luke's Hospital, University of Illinois College of Medicine, Chicago, Ill.

Read at the Thirty-fifth Annual Meeting of The American Association for Thoracic Surgery at Atlantic City, N. J., April 24 to 26, 1955.

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TABLE I. PATIENTS WITH LYMPHOMA INVOLVING THE PULMONARY PARENCHYMA

Lung Parenchyma

PATIENT	AGE	SEX	SITE	X-RAY	HISTOLOGIC DIAGNOSIS	TREATMENT	RESULTS
1. M. W. 9-45	27	F	L. Lung	Uniform density lower ⅔ left lung	Hodgkin's sarcoma	Partial resection of tumor; nitrogen mustard; x-ray	Dead, 3-54; 8½ yr. survival
2. A. F. 3-47	53	F	R. Lung	Circumscribed density, RLL, cardiophrenic angle	Lymphocytic lymphoma	Right pneumonectomy	Dead, 10-50; 3½ yr. survival. Cardiac failure
3. C. S. 1-49	70	M	L. Lung	Circumscribed density, LUL	Lymphocytic lymphoma	Left upper lobectomy	Lost to follow-up 2 yr.
4. W. J. 11-49	53	M	R. Lung	Circumscribed density, RUL	Lymphocytic lymphoma	Right upper lobectomy	Alive—well 5½ yr.
5. I. W. 4-49	24	F	R. Lung	Density—right lung cavitation and fluid level	Reticulum-cell sarcoma	Right pneumonectomy	Alive—well 5½ yr.
6. M. S. -49	25	F	Bilateral	Multiple nodular densities	Hodgkin's disease	Node biopsy; x-ray; nitrogen mustard	Alive 5½ yr.
7. G. C. 11-53	46	F	L. Lung	Circumscribed density, LLL	Lymphocytic lymphoma	Left lower lobectomy	Alive—well 1 yr. 4 mo.

TABLE II. PATIENTS WITH PLEURAL FLUID AS THE PRIMARY ROENTGEN FINDING

Pleural Fluid

PATIENT	AGE	SEX	SITE	X-RAY	HISTOLOGIC DIAGNOSIS	TREATMENT	RESULTS
8. C. D. 7-42	48	M	Right pleura, Left lung	Fluid and density, right chest Density; left lung	Lymphocytic lymphoma	Partial removal; x-ray	Alive—well 13 yr.
9. E. H. 12-47	43	F	Pleural fluid, left	Density, left chest	Hodgkin's disease	X-ray; nitrogen mustard	Dead, 7-51; 3½ yr. survival
10. I. E. 12-49	40	F	Pleural fluid, left	Density, left chest	Lymphocytic lymphoma	X-ray; nitrogen mustard: drainage of empyema	Dead, 2-55; 5½ yr. survival
11. T. M. 10-53	67	F	Right pleura, mediastinum	Pleural density	Hodgkin's disease	Thoracotomy; x-ray; nitrogen mustard	Dead, 2-55; 1⅓ yr.
12. V. D. 11-53	50	F	Right pleura mediastinum	Pleural density Mediastinal enlargement	Lympocytic infiltration of pleura	Repeated aspirations; nitrogen mustard; x-ray	Dead, 4-54; 5 mo.

Physical examination revealed an emaciated, pale, white woman who appeared chronically ill and had a temperature of 102° F. There was an enlarged node in the left cervical region and on the left side of the chest dullness was elicited in the lower half. Breath sounds were absent in the corresponding area.

The laboratory data revealed the red blood count 2.2 million, with a white blood count of 13,900 and hemoglobin, 6.4 Gm. Sputum and bronchoscopic secretions were negative for tubercle bacilli.

X-rays of the chest over a 7-month period revealed a gradually increasing density in the left lung field which, at the time of admission, occupied two-thirds of the left chest (Fig. 1).

Bronchoscopy was noncontributory and a needle aspiration yielded a small amount of blood-tinged fluid but no pus was obtained.

An antero-axillary incision was made on the left side, a portion of two ribs was removed and a pocket lined by soft necrotic and fibrinlike tissues was entered. It could not be determined whether this was in the lung or between the lobes and, after sizable portions of tissue were removed, the wound was packed wide open with penicillin gauze. The pathologic examination revealed nodular gray tissue with a microscopic appearance of great variation. Much necrosis was seen along with cellular areas containing fibroblastic proliferation, variable-sized mononuclear cells, lymphocytes, and multinucleated cells. Tubular remnants of bronchioles could be seen surrounded by sheets of large mononuclear cells some of which were in mitosis.

The interpretation of the slide was that of an epithelial neoplasm although at the time one of us (R. J. J.) thought the lesion was Hodgkin's disease. This opinion was partially corroborated at the University of Illinois, where the opinion was expressed that it was Hodgkin's sarcoma (Fig. 3).

The patient received x-ray therapy and was discharged six weeks after admission. The complete clearing of the left lung did not occur until September, 1946 (Fig. 2).

The patient has had two children since but, at the time of the second pregnancy, she developed nodes in the right cervical area and received x-ray therapy. Because of recurrence of chest pain and shortness of breath, a therapeutic abortion was performed in 1951, following a third pregnancy. At this time, chest x-ray revealed a widening of the mediastinal shadow.

In July, 1953, fluoroscopy revealed further enlargement of mediastinal widening and nitrogen mustard was given.

The last admission was in March, 1954, at which time the patient was markedly icteric, emaciated, and preterminal. She died and the autopsy revealed tissue involvement of the retroperitoneal and mediastinal areas, pancreas, spleen, kidney, adrenal glands, and lungs. The interpretation was reticulum-cell lymphosarcoma but the tissue sections demonstrated pronounced areas of fibrosis with but few scattered areas of cellular infiltration resembling that seen in the surgical specimen. These changes resembled the so-called "burnt out" Hodgkin's disease (Fig. 4).

CASE 2.—February, 1947. The patient (A. F.), a 59-year-old white woman, had complained of a mild, dry cough, decreased appetite, and weakness for four to five months. Spicy foods had caused "stomach distress" following eating but gastrointestinal x-rays were negative. The chest roentgenograms revealed a dense, fairly well-demarcated mass in the right lower lobe at the cardiophrenic angle.

The laboratory data revealed a RBC of 3.7 million; with hemoglobin, 11.5 Gm.; and WBC, 5,900. The differential count was normal and urine and Wassermann tests were negative. Sputum specimens were scant and negative for tubercle bacilli.

Bronchoscopic examination revealed compression of the right lower lobe bronchus and aspiration of the posterior basilar segment yielded a small amount of clotted blood.

Thoracotomy was done at which time a lemon-sized mass was felt in the lower lobe. The overlying pleura was slightly puckered and the impression was that the lesion was carcinomatous. The lung along with lymph nodes at the hilus was removed and the convalescence was uneventful.

The pathologic examination revealed a firm mass in the lower lobe which on cut surface had an irregular, indistinct border of gray color with flecks of carbon pigment. It had occupied slightly less than one-third of the collapsed lower lobe. The lymph nodes were mainly anthracotic.

Microscopically, the sections consisted of numerous small lymphocytes infiltrating the lung parenchyma and obliterating all the architecture with the exception of remnants of bronchi and bronchioles. The lymph nodes were negative.

Fig. 1.

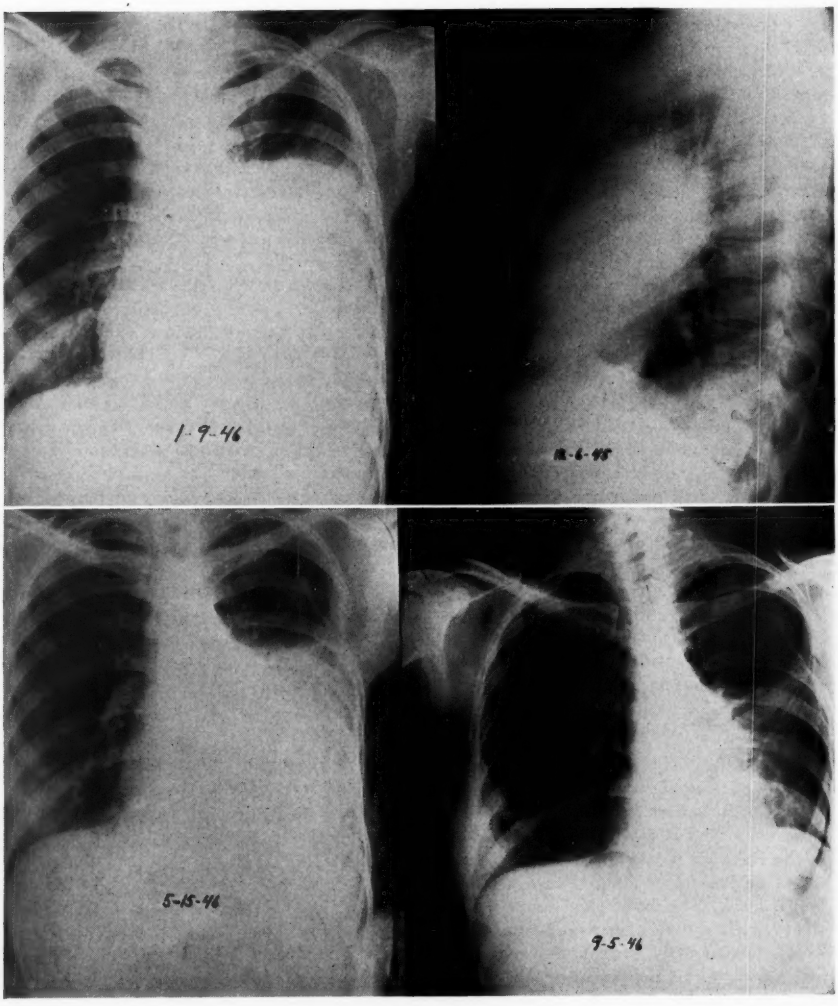


Fig. 2.

Fig. 1.—Case 1. Mass in left chest; preoperative x-ray.
Fig. 2.—Case 1. Postoperative chest x-rays. Clearing of process in lung required seven months.

The final diagnosis was small-cell lymphosarcoma.

The patient re-entered the hospital three months later because of slight difficulty in breathing and swallowing accompanied by occasional palpitation. She was given a course of nitrogen mustard.

Fig. 3.

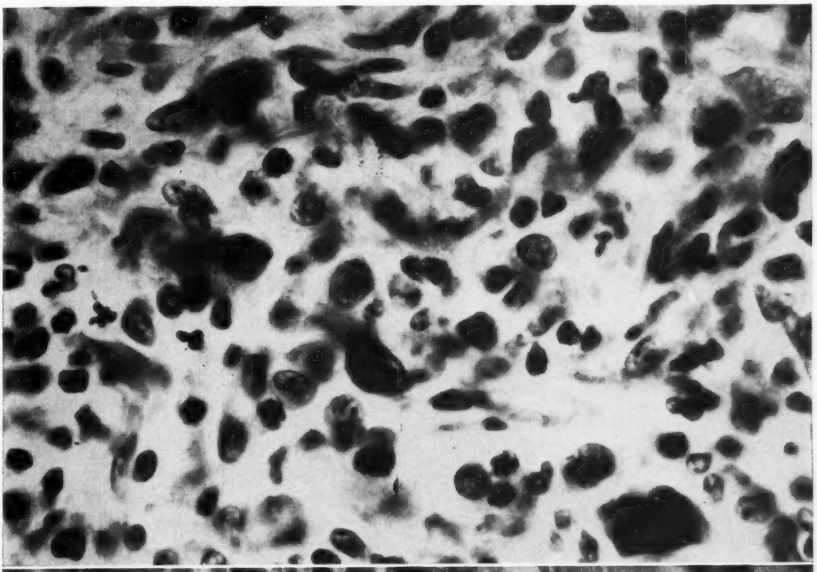


Fig. 4.

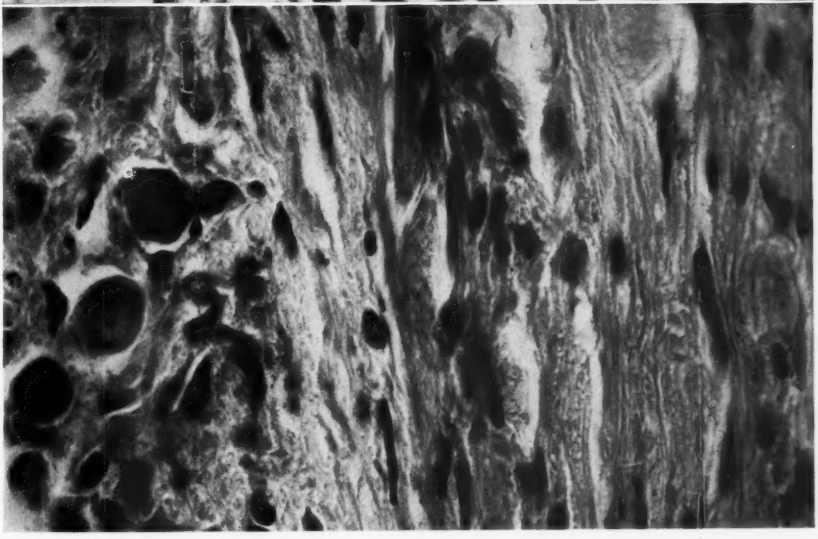


Fig. 3.—Case 1. Surgical specimen—pleomorphism and many giant cells—Hodgkin's sarcoma.

Fig. 4.—Case 1. Autopsy specimen—8 years later. Pronounced connective tissue proliferation; degenerative changes in tumor infiltrate.

The patient was not seen again. Death occurred in October, 1950, and the records of the referring doctor stated that it was due to cardiac failure.

CASE 3.—November, 1948. The patient (C. S.) was a 70-year-old white man, who entered the hospital with complaints of shortness of breath which had increased in severity during two years and a cough, of two months' duration, productive of whitish phlegm streaked with blood. He had been hospitalized one week elsewhere because of a diagnosis of pneumonia and was improved but entered St. Luke's Hospital at this time because of the persistent blood-streaked sputum and because of an abnormal shadow seen in the chest x-ray. Two years before the patient had been hospitalized because of a heart attack and since then had had occasional precordial pain on exertion.

The physical examination revealed a somewhat short, stocky, elderly white man in no apparent distress. There were no enlarged lymph nodes in the cervical, axillary, or inguinal regions. The heart and lungs were normal, and the blood pressure was 130/80. There was a left inguinal hernia which could be reduced and a large soft tumor mass in the lumbar region, extending on both left and right sides, which was thought to be a lipoma.

The laboratory studies revealed negative serology and a slight trace of albuminuria. The RBC was 4.2 million; hemoglobin, 12.9 Gm.; and the WBC, 9,300. The nonprotein nitrogen was 44 mg. per cent.

The chest x-ray revealed a solitary density in the left upper lobe just lateral and superior to the hilus. It was not sharply circumscribed, having an irregular border which merged into the adjacent lung tissue. An x-ray two months later revealed no appreciable change.

Bronchoscopy revealed slight compression of the upper lobe and broadening of the spur between the lingula and upper segmental bronchi. Biopsy was taken from the area and secretions aspirated for cytologic study, both of which were negative for tumor. The patient was discharged after the bronchoscopy but readmitted in two months because of the persistence of the hemoptysis. Repeat chest x-rays revealed no appreciable change.

A thoracotomy was done, at which time a firm mass was felt in the left upper lobe. Although it was thought likely to be a carcinoma, only the upper lobe was removed because of the patient's age and previous coronary history. The patient had an uneventful convalescence and was discharged two and one-half weeks postoperatively.

The pathologic examination revealed a mass, measuring 4.5 cm. in greatest diameter and having a gray cut surface with scattered areas of black. Microscopically, the lung tissue was replaced by dense masses of small lymphocytes. These areas were not arranged in follicles and did not have a sinusoid pattern but replaced the parenchyma and surrounded the small bronchi, bronchioles, and vessels which could be identified. The pathologic diagnosis was lymphosarcoma (small-cell) of the lung.

The patient was seen two years later, at which time there was no evidence of recurrence and the chest x-ray revealed good expansion of the remaining lower lobe. He has been lost to follow-up.

CASE 4.—October, 1949. The patient (W. J.), a 53-year-old Negro man, had complained of slight shortness of breath and a cough for the previous two years with a gradual increase in symptoms accompanied by the development of mucoid expectoration in the past four to six weeks. He had had one episode of blood-streaked sputum about a year before. A mobile unit x-ray film taken in September, 1949, revealed an abnormality in the right lung field and admission to Research and Educational Hospital followed.

Physical examination revealed a short, stocky Negro man in no obvious respiratory distress with normal pulse and temperature and blood pressure of 148/80. No enlarged nodes could be palpated in the cervical, axillary, or inguinal areas. Auscultation of the chest revealed dry râles in the right lung posteriorly. X-rays of the chest revealed a density in the right upper lobe which was considered to be an infarction or atypical pneumonitis.

Bronchoscopy was done on two occasions and revealed a compression and stenosis of the right upper lobe orifice.

Thoracotomy was done in November, 1949, at which time a firm mass was found in the upper lobe along the major fissure. The lobe was smaller in size and on positive pressure no expansion of the area occurred. Because of the reported stenosis, the upper lobe was removed. The patient had an uneventful convalescence.

Pathologic examination revealed a firm mass of 5 cm. in diameter in the peripheral portion of the lobe. The cut surface had a gray-pink color with scattered anthracotic patches. No point of origin could be identified in the opened bronchi.

Microscopically, diffuse infiltration of mature lymphocytic cells was seen throughout the tissues.

The final diagnosis was lymphoblastoma of the right upper lobe, low-grade lymphosarcoma form.

CASE 5.—November, 1949. The patient (I. W.) was a 24-year-old white woman who became ill in May, 1949, noting "clicking" sounds in the chest when lying down. This was followed by the development of a cough which was soon productive of green-yellow, foul-smelling material. She had pain in the right chest, vomiting attacks with the spasms of coughing, and had lost 32 pounds since the preceding July. An x-ray made in 1947 by a mobile unit was reported as negative but one made in July, 1949, was abnormal. The latter report had resulted in previous hospitalization and bronchoscopic studies (July and September, 1949).

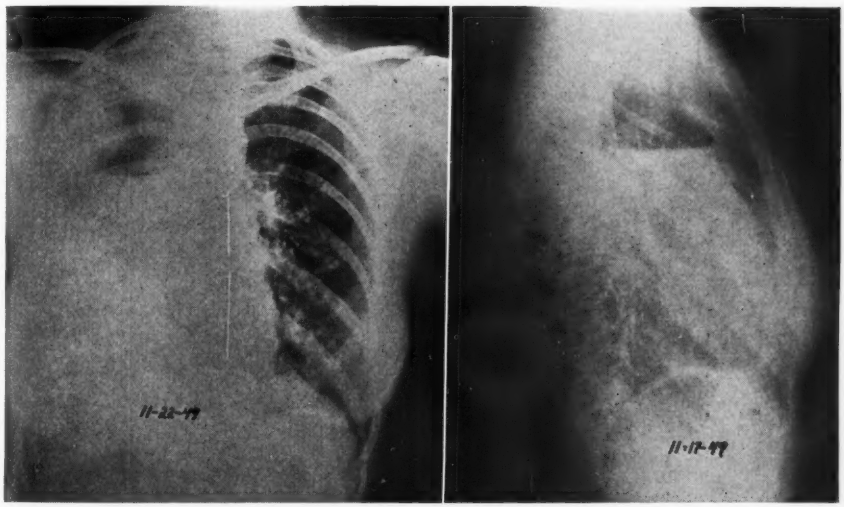


Fig. 5.—Case 5. Large cavitary lesion in upper lobe right lung. Lipiodol residue in left lung.

On physical examination, the patient appeared chronically ill with a temperature of 100° F., pulse 90, respirations 24, and there were slight clubbing and cyanosis of the fingers. There were a few small lymph nodes in the neck but no inguinal or axillary adenopathy. There was dullness over the entire right chest with many coarse bubbling râles. The liver and spleen were not palpable.

The laboratory data revealed negative urine and serology. The RBC was 3.7 million; hemoglobin, 12.2; and hematocrit, 35.5. Sputum and bronchial aspirations were negative for tubercle bacilli as was guinea pig inoculation. Secretions were negative for fungi.

Chest x-rays revealed a density occupying the upper portion of the right lung field, which gradually increased so that the entire right lung field was opaque. Subsequently, a cavity and fluid level appeared in the upper lung field which, on lateral view, corresponded to the right upper lobe (Fig. 5).

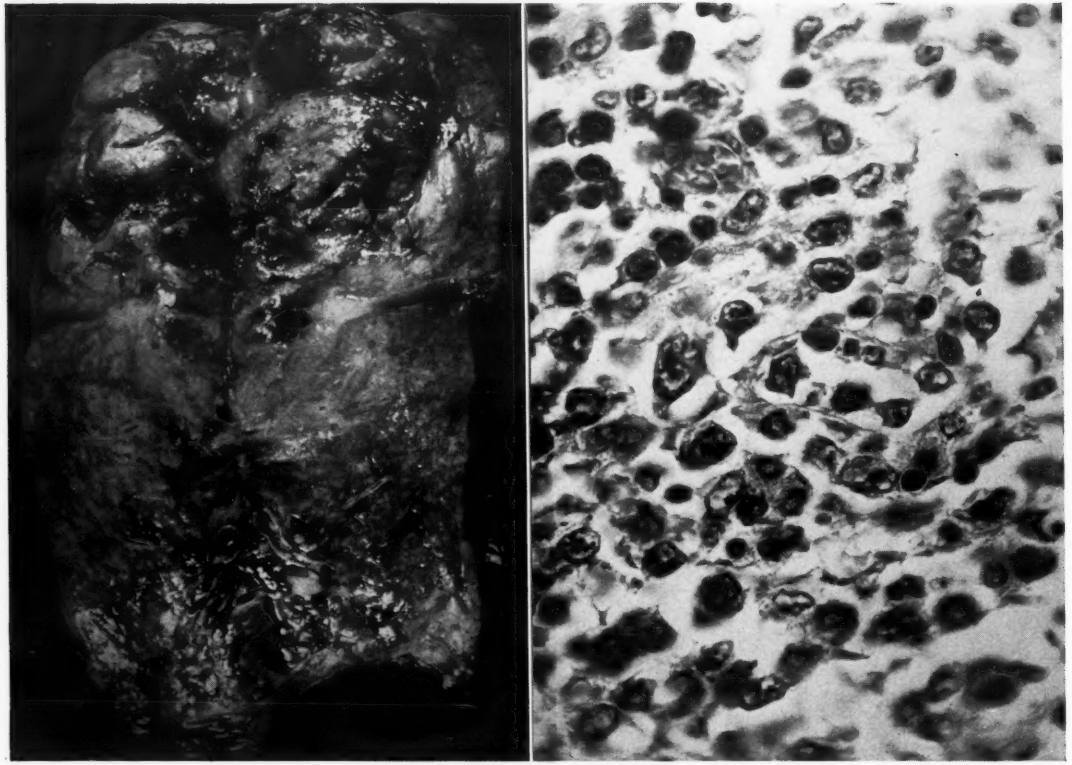


Fig. 6. Fig. 7.

Fig. 6.—Case 5. Resected right lung, cut surface. Large cavity with thick walls, upper lobe; consolidation in lower and middle lobes.

Fig. 7.—Case 5. Immature type of lymphoma. Clasmatocytoma or reticulum-cell lymphosarcoma.

The bronchoscopic reports and pathologic interpretations were as follows:

July 23, 1949: A granular, whitish mass was seen at the right side of the carina occluding entrance to the right main bronchus. The bronchoscope could not be passed beyond the mass.

Biopsy revealed fragments of hyaline cartilage and masses of necrotic tissue with ghosts of cellular structures.

Diagnosis: Necrotic tissue, in all likelihood neoplastic.

Sept. 10, 1949: A granular fungating mass was seen to arise from the right side of trachea, 1 cm. above the carina, and it encircled the orifice of the right main bronchus.

Pathology: Bits of squamous and respiratory epithelium were present. Many polys and lymphocytes were present beneath the epithelium. Areas of necrosis were present and suggestive of caseation. Necrosis was present but no acid-fast bacilli were seen.

Diagnosis: Necrosis with acute and chronic inflammation and squamous-cell metaplasia.

Oct. 29, 1949: A reddish mass partially obstructed the right main bronchus. A biopsy was taken.

Pathology: Dense connective tissue and granulation tissue were present.

Diagnosis: Reactive changes not typically inflammatory. Larger cells present and a peculiar alignment were suggestive of a lymphomatous process.

Nov. 18, 1949: Two raised areas were present 2 cm. above the carina on the right lateral wall of the trachea. The mucosa was smooth. There was a stenosis of the right upper lobe but tissue was removed from within the orifice of the upper lobe. The carina was widened.

Pathology: Hemorrhagic loose areolar and dense collagenous tissues were infiltrated with many acute and chronic inflammatory cells.

Diagnosis: Acute and chronic inflammation of the bronchus.

A thoracotomy was done on Nov. 29, 1949. Many adhesions were encountered. The entire upper lobe was firm with a fluctuant central area. The entire lung was removed with closure of the bronchus at the carina (Fig. 6).

The patient made an uneventful recovery and on the second week postoperatively was given a course of nitrogen mustard therapy at the end of which time she was discharged from the hospital.

The pathologic examination revealed a large cavity 10 cm. in diameter in the upper lobe. The lining of this consisted of ragged, ulcerated, tan and gray tissues. There was a defect at the hilus, which communicated directly with the cavity, the wall of which was as large as 3 to 4 cm. in thickness and resembled "fish flesh" in appearance.

The middle and lower lobes were adherent by dense adhesions and on cut surface the bronchi and bronchioles contained creamy exudate. The nodes at the hilus were enlarged and firm.

Histologically, much of the lung tissue was necrotic, pink, amorphous material. There were many scattered areas consisting of very pleomorphic large and small cells invading the atelectatic parenchyma. Some were multinucleated and giant in size. The lymph nodes contained many inflammatory cells.

Diagnosis: Lymphoblastoma of right upper lobe with extensive necrosis; acute bronchitis and chronic bronchopneumonia; and hyperplasia of hilar nodes (Fig. 7).

This patient is alive and well at present, almost five and one-half years since surgery, and has had three children since then.

Fig. 7.—Case 5. Immature type of lymphoma. Clasmatocytoma or reticulum-cell lymphosarcoma.

CASE 6.—October, 1949. The patient (M. S.), was a 25-year-old white woman, a housewife, who entered St. Luke's Hospital with a history of generalized itching, swelling of the right side of the neck and a weight loss of 10 to 12 pounds during the previous six months. Following x-ray studies of the chest in August, the patient had entered a tuberculosis sanatorium where streptomycin therapy was given for eight weeks' time (Fig. 8). Despite treatment, there was a progressive increase in the number and size of the nodules and she was transferred for further work-up.

The physical examination revealed a young white woman with numerous areas of excoriation from scratching over most of the body surface.

There were several 2 to 3 cm. firm nodes palpable in the right cervical region and a few pea-sized nodes on the left side. The lungs and heart were essentially normal with the blood pressure of 135/70. The abdomen was negative.

The laboratory data revealed negative urine and negative serology with a RBC of 3.46 million, a WBC of 16,400, and hemoglobin of 10.3 Gm.

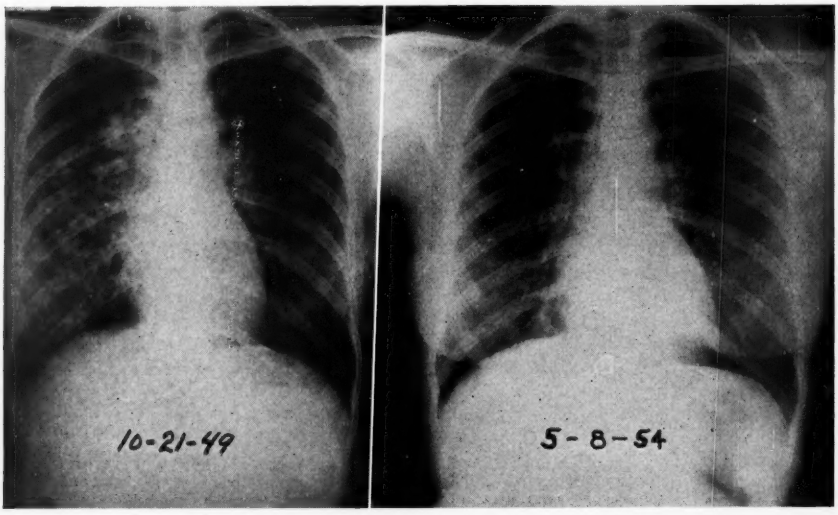


Fig. 8.—Case 6. Nodular dissemination of Hodgkin's disease. First interpretation was pulmonary tuberculosis.

There were finely mottled, soft densities scattered throughout the right lung field with only faint suggestion of left lung involvement. An x-ray in October revealed coalescence, enlargement, and increase in these areas. A chest film in 1954 revealed almost complete disappearance of the pulmonary infiltrations.

A cervical node on the right side was removed, and the histologic diagnosis was Hodgkin's disease. The patient received nitrogen mustard for four consecutive days.

The second admission was in February, 1952, because of edema of the left lower extremity and lymph node enlargement in the inguinal area. She received another series of nitrogen mustard treatments on four consecutive days.

The patient has not been seen since 1952 but she is still alive. Personal communication with the family doctor revealed that the patient has had several repeated series of both x-ray and mustard treatments.

CASE 7.—December, 1953. The patient (G. C.) was a 46-year-old white woman who had had an abnormality discovered in an x-ray of her chest made by a Mobile Survey Unit, six weeks before entrance to St. Luke's Hospital. She had had previous films made which had been reported as negative. She was essentially without complaints except for slight fatigue.

The physical examination failed to reveal any essential abnormality. No palpable nodes were present in the neck, axillary, or inguinal area. The heart and lungs were normal. Blood pressure was 120/80. Liver and spleen were not palpable.

The laboratory findings revealed negative urine and serology. The RBC was 4.8 million; WBC, 8,300; hemoglobin, 12.6, with lymphocytes 6, monocytes 4, neutrophils 83, and bands 7.

The chest x-rays are shown in Fig. 9.

Bronchoscopic examination revealed slight injection of the mucosa in the left lower lobe bronchus but no masses or compression of the segmental orifices. Aspiration deep in the lower lobe bronchus caused pronounced oozing from the bronchus and this material was sent for Papanicolaou and cell block studies, both of which were negative.

At thoracotomy, a firm mass was found in the left lower lobe and on the interlobar surface the pleura had a brown discoloration, suggesting an infarction. Several small nodes were present along the bronchus and these were removed with the entire lower lobe.

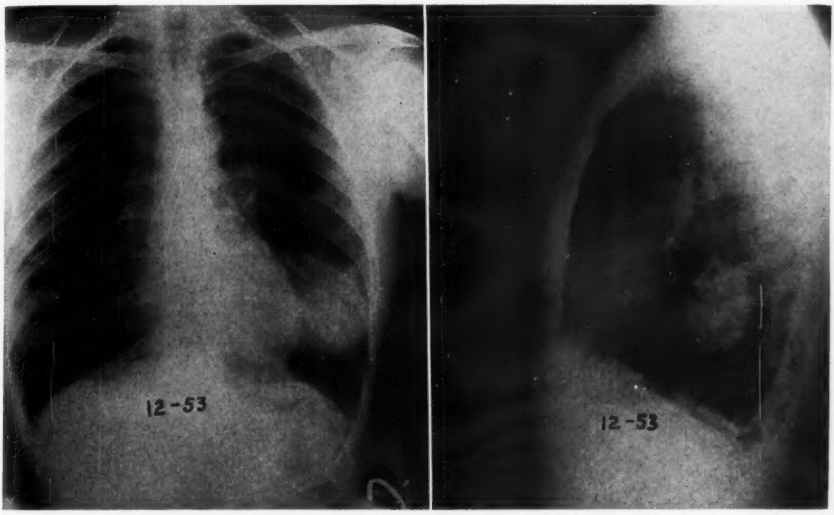


Fig. 9.—Case 7. Solitary mass in lower lobe of left lung.

The pathologic examination revealed a mass which measured 7 cm. in greatest diameter on cut surface and had a grayish-tan color (Fig. 10). No distinct point of bronchial origin was found. Histologically, the mass consisted of many small lymphocytes without distinct sinusoids or cortical nodules. These surrounded bronchi, bronchioles, and small vessels and contained scattered carbon deposits. The cells replaced the alveolar lung parenchyma and the pathologic diagnosis was small-cell lymphosarcoma (Fig. 11).

The resected lymph nodes were negative. The convalescence was uneventful, and the patient is alive and well almost eighteen months following surgery.

Case 8.—July, 1942. The patient (C.D.) was a 48-year-old white man who entered St. Luke's Hospital in July, 1942, for bronchoscopic study and evaluation of an abnormality in a chest x-ray taken when he attempted to obtain a commission in the Armed Forces. Other than occasional cough and slight expectoration associated with colds, he felt that he was entirely well.

The physical examination was entirely within normal limits except for slight generalized obesity. The laboratory data were within normal limits and bronchial secretions were negative for tubercle bacilli.

Fig. 10.

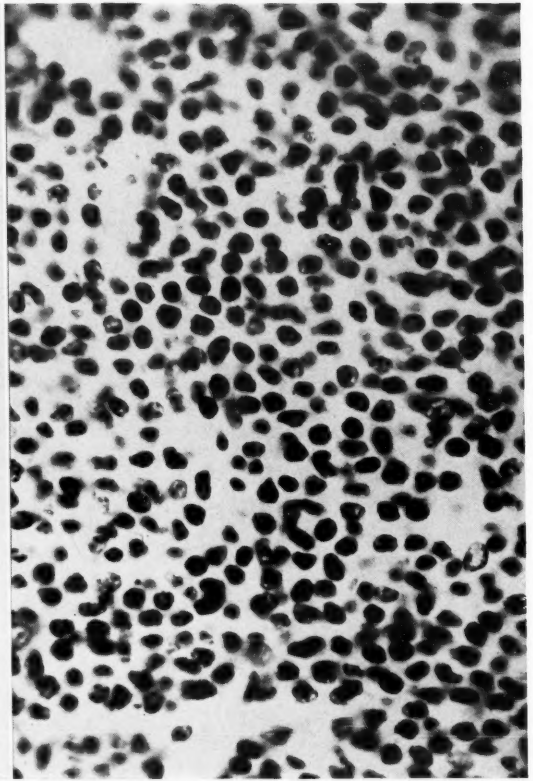


Fig. 11.

Fig. 10.—Case 7. Cut surface of lower lobe. The tumor was homogeneous, bulging and had fine irregular margin.

Fig. 11.—Case 7. Lymphocytic lymphoma. The majority of cells are fairly mature; occasional lymphoblasts present.

The chest x-rays revealed a fusiform density at the lateral chest wall opposite the fourth through sixth ribs laterally and a soft nodular ill-defined density opposite the left pulmonary hilus.

Bronchoscopic studies were essentially normal.

The second admission was in October, 1947, at which time the patient complained of slight shortness of breath. The chest x-rays (Fig. 12) revealed enlargement of the density on the left side, a new density in the right lung extending from the first to third ribs anteriorly and obliteration of the lower half of the right lung field, suggesting fluid. Thoracentesis was done and 2,300 c.c. of slightly turbid, yellow fluid was obtained. Histologically, this was reported as pleural exudate but the majority of the cells were lymphocytes.

The third admission was in July, 1948, at which time the patient had marked dyspnea and a temperature of 104° F. During the past months, fluid had been removed at monthly intervals totalling about 6 L. Since the last aspiration, he had developed fever and pronounced dyspnea. Twelve hundred cubic centimeters of slightly turbid fluid were removed from which hemolytic *Staphylococcus aureus* was cultured.

The chest x-rays at this time were essentially the same as of October, 1947 (Fig. 13), except for an increase in the size of the lesions in both chest cavities and the appearance of a third lesion in the costophrenic angle on the right side above the fluid level.

A right thoracotomy was done in August, 1948. The two larger areas were extrapleural in location and consisted of "soft fatlike tumor" with minute cystic spaces. A frozen section of this was reported as small-cell or round-cell carcinoma. The lower mass consisted of fibrin and extended between the lobes. The remaining pleura over the lower and middle lobes had the appearance of a pyogenic membrane and restricted the complete examination of the lung. The extrapleural masses were resected, the fibrin and exudate from the pleural space was removed, and decortication of the lower and middle lobes was done. The chest was closed with intercostal drainage.

The tissue submitted for pathologic examination consisted of several portions, the largest measuring 8 by 7 by 2.5 cm. It had a soft consistency with a gray and tan-brown cut surface. Histologically, the tissue was composed of lymphocyte-like cells, having very little cytoplasm and a vesicular nucleus. Very little stroma and only an occasional germinal center were present (Fig. 14).

The hospital course was prolonged because of the persistence of the pleural space infection, and the patient was finally discharged with a residual pocket of about 90 c.c. in size. During the hospitalization, he received roentgen therapy over the right thorax following which there was complete disappearance of the lesion in the left chest as well.

The fourth hospital admission was in November, 1948, at which time the pleural pocket was unroofed removing a portion of two ribs. Pathologic examination of the thickened parietal pleura did not reveal any evidence of lymphosarcoma at that time.

In November, 1953, the patient developed diarrhea and blood in the stools, and on proctoscopic examination an adenocarcinoma was found at the 12 cm. level on the anterior aspect of the rectum. An abdominoperineal resection was performed by Dr. Pontius and was followed by an uneventful convalescence.

In February, 1954, the patient had an episode of blood-streaked sputum. An x-ray (Fig. 15) revealed the rib defects from the open drainage procedure on the right side and an ill-defined mass off the left hilus in the area of the previous mass in the left lung.

Bronchus examination revealed the bleeding source to be in the right lower lobe. The left side was entirely normal. The pathologic study revealed only hemorrhagic bronchial fluid.

Roentgen therapy was again given over the left chest and the last x-ray, March, 1954 (Fig. 15), demonstrated disappearance of the mass in the left lung. Bronchoscopy was repeated in March because of the persistence of the blood-streaked sputum and again confirmed the site of the bleeding in the lateral basilar bronchus of the right lower lobe. Cell block and Papanicolaou examinations were negative for tumor.

The bleeding disappeared after antibiotic therapy and since March, 1954, there has been no recurrence.

Fig. 11.—Case 7. Lymphocytic lymphoma. The majority of cells are fairly mature; occasional lymphoblasts present.

The patient is alive and well at the present time, thirteen years after the first known evidence of lymphosarcoma, having undergone surgical and roentgen therapy for it, plus a cholecystectomy at another hospital and an abdominoperineal resection for adenocarcinoma of the rectum in that time.

CASE 9.—December, 1947. The patient (E. H.) was a 43-year-old white woman who had had pneumonia five months previously and had been treated at another hospital with

Fig. 12.

Fig. 13.

Fig. 12.—Case 8. Enlargement of pulmonary shadows with pleural fluid; five-year interval.

Fig. 13.—Case 8. Postthoracentesis. Mass on left is in left lung; nodules on right are extrapleural.

antibiotic medication. Following this, she had a persistent cough, expectorated thick, brownish material, and had episodes of fever. She was "anemic" for which liver medication was given. She developed hemoptysis and was rehospitalized where x-ray studies of the chest suggested fluid in the left pleural cavity. She was admitted to St. Luke's Hospital in December for bronchoscopic study and evaluation.

Physical examination revealed changes in the left chest suggestive of fluid and there were enlarged lymph nodes present in the right cervical and right inguinal regions.

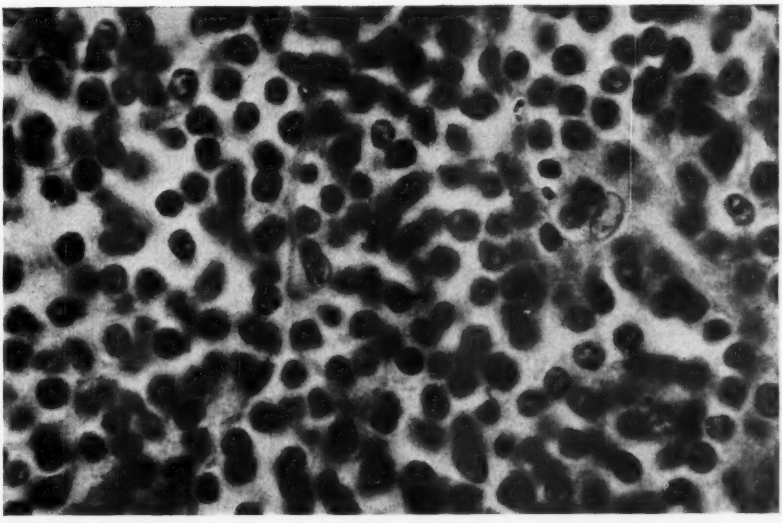


Fig. 14.—Case 8. Lymphocytic lymphoma. Cells are immature lymphocytes.

Fig. 15.—Case 8. Recurrence of mass in left lung and clearing following x-ray irradiation.

The laboratory data revealed RBC, 3.8 million; WBC, 8,100; and hemoglobin, 11.5 Gm. The urine and serology were negative, and the sputum was negative for tubercle bacilli.

The x-ray studies demonstrated the left pleural cavity to be obliterated except for a small area of aerated lung at the apex.

The bronchoscopic examination revealed a broadened carina and compression of the left main bronchus. Stenosis was present at the upper lobe orifice and the mucosa was thickened and friable. Biopsy was obtained from this area and the report was questionable lymphosarcoma of the bronchial mucosa.

Fluid was aspirated from the chest and, histologically, showed numerous lymphocytes.

A biopsy of an inguinal node was done and the histologic report was small-cell lymphosarcoma.

She re-entered the hospital in July, 1949, because of swelling of the lower extremities. Physical examination revealed swelling of both lower extremities, more marked on the right, and a recurrence of nodes in the right inguinal area. The patient received x-ray therapy. Chest x-ray revealed no recurrence of fluid or widening of the mediastinum.

She was readmitted in December, 1949, because of persistence of swelling in the right thigh. At this time, nitrogen mustard was given and improvement in the swelling occurred.

In February, 1951, she was readmitted because of back pain and swelling in the neck. Treatment consisted of x-ray therapy to the neck and lumbar spine and there was improvement but the cervical nodal enlargement recurred and more x-ray was given in May, 1951.

Her last admission was in June, 1951, when she was preterminal. Mustard therapy was given but no improvement followed. The patient died in July, 1951, slightly less than four years after the onset of the disease.

Review of lymph node biopsy revealed a very abnormal cellular pattern. The cells were variable in size and shape and scattered eosinophils were present. A very occasional, large, double nucleated cell was seen suggesting Sternberg-Reed-cells. Necrosis was not apparent. The diagnosis was finally made of early Hodgkin's disease without necrosis or fibrosis.

CASE 10.—December, 1949. The patient (I. E.) was a 40-year-old white woman who had developed pleurisy on the right side six months before and two months previously had noticed difficulty in breathing. She had been treated elsewhere and clear or slightly blood-tinged fluid had been aspirated from the left chest several times.

On physical examination, no enlarged nodes were palpable but dullness to percussion and absent breath sounds were the abnormal findings on the left side.

Laboratory studies revealed negative urine and serology. RBC was 4.1 million; WBC, 8,300; and hemoglobin, 12.9 Gm. The differential count was lymphocytes 6, monocytes 4, neutrophils 75, basophils 2, eosinophils 8, bands 5. The aspirated fluid was negative to smear and culture.

Treatment consisted of thoracentesis on two occasions, removing 1,500 c.c. of clear, straw-colored fluid and, two weeks later, 2,400 c.c. of light brown fluid. Between these two aspirations, a course of nitrogen mustard was given.

Pathologically, the fluid contained numerous lymphocytes and the diagnosis of the blocked centrifuged specimen was of marked lymphocytic infiltration of pleural fluid.

The patient re-entered the hospital a year later because of recurrence of fluid and 1 L. was again removed. The histologic report again was of marked lymphocytic infiltration of pleural fluid, and the patient received another course of nitrogen mustard.

In 1952, following aspiration of recurrent fluid, the patient developed a hemolytic *Staphylococcus aureus* empyema, which was treated by aspiration and antibiotic therapy. Surgical drainage was not done because of the associated lymphosarcoma and the patient was discharged with a residual density in the left lower chest. She received x-ray therapy over the left chest (Figs. 16 and 17).

In October, 1954, the patient was admitted because of persistent fever and pain. Needle aspiration revealed thick pus and thoracotomy drainage was accomplished under local anesthesia.

The thickened parietal pleura was submitted for histologic examination and revealed a dense layer of lymphocytic infiltration on one side of the collagenous tissue with a pyogenic layer on the opposite side (Fig. 18). Pathologic diagnosis was lymphosarcoma of the pleura.

The patient was hospitalized two more times in 1955 for nitrogen mustard therapy and x-ray therapy but she died in February, 1955, five and one-half years after the onset of her symptoms. Permission for an autopsy was denied.

Fig. 16.

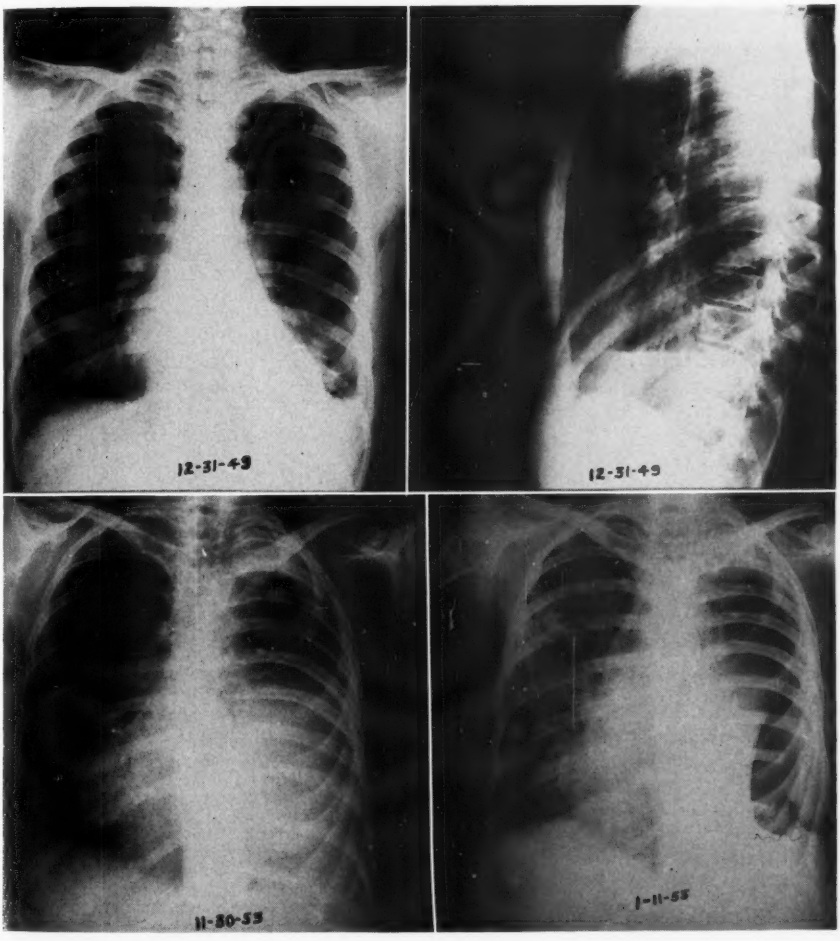


Fig. 17.

Fig. 16.—Case 10. Postthoracentesis x-rays of chest.

Fig. 17.—Case 10. Residual empyema pocket, left chest and postthoracotomy film; spread of lymphoma to right lung.

CASE 11.—October, 1953. The patient (T. M.) was a 67-year-old white woman who had noticed weakness and slight shortness of breath and had been treated elsewhere for heart disease. Because of the increase in her dyspnea, examination and x-rays of the chest by another physician suggested fluid in the right pleural cavity. She entered St. Luke's Hospital, where the essential physical findings were limited to the right pleural cavity and suggested the presence of fluid. The heart was shifted to the left and had a normal sinus rhythm, and the blood pressure was 170/94. The liver was enlarged four fingerbreadths below the costal margin.

The laboratory studies revealed a normal urine and serology. The RBC was 4.5 million; WBC, 4,900; and hemoglobin, 13.2 Gm.

Chest x-rays revealed a density in the right chest, suggesting fluid. Aspiration of the chest was done on two occasions, and 2,400 and 1,600 c.c. of slightly opalescent, straw-colored fluid were obtained.

Fig. 18.—Case 10. Hyalinized connective tissue of pleura with dense infiltration of lymphosarcoma above.

The histologic study revealed many lymphocytes, and the diagnosis was submitted as lymphocytic infiltration of pleural fluid. The second fluid specimen revealed similar lymphocytes but to a lesser degree.

Bronchoscopic examination revealed minimal increased redness of the mucosa but no evidence of bronchial compression or changes of the coryna. The aspirated secretions were negative for carcinoma (Papanicolaou and cell block study).

A thoracotomy was done and 1,500 c.c. of fluid removed. There was slight injection of the parietal pleura but no nodular masses were present on the pleura. There were confluent, firm nodes below the right main bronchus extending downward into the pulmonary ligament. Two nodes were present above the azygos vein and a walnut-sized mass was present above the diaphragm. Several of the nodes and the mass above the diaphragm were removed, and on histologic examination were reported as either reticulum-cell lymphosarcoma or Hodgkin's disease.

The patient was given nitrogen mustard after a suitable period of convalescence.

Readmission was six months later (June, 1954). She had received x-ray therapy for enlarged nodes in neck, axilla, and inguinal area. She also had developed pain in the left leg and hip and required a crutch for walking. She was given another course of nitrogen mustard in June and in October, 1954. She died in February, 1955, at home, and permission for an autopsy was not obtained.

The final reclassification of the node pathology was Hodgkin's disease.

CASE 12.—November, 1953. The patient (V. D.) was a 50-year-old white woman who had complained of a gradual increase in shortness of breath and a nonproductive cough for the preceding four months. She was treated with digitalis and diuretics by her family doctor but her complaints increased. After x-ray studies revealed fluid in the right pleural cavity, thoracentesis was done which yielded 500 c.c. of fluid on one occasion and three weeks later, 1 L. of slightly blood-tinged fluid was aspirated. The patient had had acute rheumatic fever as a child of 13.

The physical findings were essentially confined to the right chest, where changes indicative of pleural fluid were elicited. The heart was normal in rhythm and rate with a blood pressure of 138/80. A few small nodes were palpable in each axilla.

The laboratory findings revealed a RBC of 4.9 million; WBC, 10,400; and hemoglobin, 14.3 Gm. The differential count was lymphocytes 24, monocytes 3, polymorphonuclear leukocytes 60, eosinophils 4, and bands 9.

X-rays of the chest revealed obliteration of the lung markings by fluid.

Approximately 1,500 c.c. of amber fluid were removed from the right pleural cavity. Following aspiration, a fusiform widening of the right side of the mediastinum was seen. Histologic examination of the blocked centrifuged specimen revealed myriads of lymphocytes and the suggestion of the pathologist was that the patient might have a lymphoma. Three small nodes were removed from the axilla and were negative histologically. She was given nitrogen mustard for four consecutive days and a chest x-ray subsequently revealed narrowing of the mediastinum and only a small amount of fluid in the pleural cavity.

She was readmitted five weeks later complaining of shortness of breath and swelling of the ankles. Fluid was aspirated from the chest twice, six and twelve days later.

Two liters of fluid was removed which had the same histologic findings. Chest x-ray revealed marked mediastinal widening and hydropneumothorax. Following this, roentgen therapy was given.

She was readmitted six weeks later with complaints of shortness of breath, anorexia, weight loss, and diplopia. The chest contained fluid, the liver and spleen were enlarged, nodes were present in the neck and there was a lateral deviation of the right eye. The right chest was aspirated and 2,200 c.c. of fluid was obtained. Nitrogen mustard therapy was repeated and the patient was discharged with questionable improvement.

Death occurred in April, 1954, at home and permission for autopsy was not obtained.

DISCUSSION

Analysis of this group revealed that the symptomatology was absent, minimal, or pronounced. At least 3 patients had silent pulmonary shadows, 1 had occasional blood-tinged expectoration, and 2 had overwhelming symptoms of toxemia with anemia, fever, severe cough with varying degrees of productivity, and marked weight loss. As would be expected, shortness of breath was the chief complaint of those in the pleural fluid group. The age group varied from 24 to 70 years but there was a definite tendency toward a young age incidence. Two of the patients, who were in the third decade, had Hodgkin's disease which has a tendency toward early occurrence in life (Gall and Mallory[3]).

The sex incidence was in contrast to that in the collected series of Beck and Reganis.[8] Seventy-five per cent of the patients were women.

The roentgenologic changes similarly were extremely variable although a circumscribed density was present in 4 patients. One of the patients with pleural fluid had two densities which were extrapleural on the same side and a density in the contralateral lung. Two patients had massive pulmonary involvement, in 1 of whom bronchial occlusion, consolidation, and abscess formation were present. A disseminated nodular disease present in both lungs but primarily on the right side was seen in 1 patient in this group. This corresponded to the Class II type reported in Robbin's roentgenographic study, which group incidentally comprised over 85 per cent of the reported cases.

The patients with pleural fluid all exhibited typical fluid shadows, and in 1, mediastinal changes subsequently occurred.

Examples of the variations in roentgenologic appearance accompany the briefs of the case histories.

Likewise, the bronchoscopic findings are listed in the abstracted histories. For the most part, information obtained was limited. One patient was bronchoscoped four times prior to resection and with biopsy material obtained on one of these occasions changes suggesting a lymphoma were reported. One patient in the pleural fluid group had a biopsy of the wall of the left main bronchus, the site of compression at the left upper lobe orifice, and this revealed lymphocytic infiltration of the bronchial mucosa, possibly lymphosarcoma. These two instances were the only examples in the series in which diagnosis was suggested by bronchial material. In the remainder, negative reports or instances of varying degrees of bronchial compression were described.

Of particular interest were the pathologic findings. Four patients in the resected group had a solitary mass which varied from a few centimeters up to 8 to 10 cm. in greatest diameter. These were firm, rubbery in consistency, and had a bulging cut surface varying from pinkish-gray to tan-gray color. The margins in most instances were finely irregular and what might be described as fuzzy, blending into the surrounding parenchyma. The tumor mass could not be enucleated from the lung; however, the masses of tumor which were resected in Case 8 were separated from the extrapleural tissues by a fairly distinct line of cleavage. This tumor tissue also had a gray and tan cut surface.

One resected specimen contained a large abscess cavity and almost the entire upper lobe was involved. Again the cut surfaces had a pink-gray color and the pathologist chose the term "fish flesh" in describing it.

The most common histologic type was the lymphocytic lymphosarcoma. Microscopically, there was a diffuse infiltration of small lymphocytic cells without semblance of normal lymphoid architecture. Sinusoids, trabeculae and germinal centers were totally lacking but remnants of small bronchi, bronchioles, and vessels could be identified. There were occasional less differentiated cells which appeared as larger cells with a more vesicular, less heavily stained nucleus and occasional nucleolus, which could be interpreted as lymphoblasts.

The solitary tumor lesions in 4 patients were of this type. In one patient with extrapleural masses and pleural fluid, the tumor pathology in the contralateral lung also was of this type and Case 10, a patient with recurring pleural

fluid, demonstrated the identical histologic changes in the thickened scar tissue excised from the parietal pleura. The photomicrographs in Figs. 11 and 15 are of this histologic type.

The histologic picture of the lung resected in Case 5 was that of a very immature type cell, large, variable in size and shape, and in some instances having cytoplasmic processes extending from the cells (Fig. 7). The nucleus contained scant chromatin and frequently nucleoli were apparent. Considerable necrosis with a variegated assortment of scattered polymorphonuclear and mononuclear inflammatory cells were also seen.

Although this was classified as a lymphoblastoma, it would be more in keeping histologically with a clasmatocytoma (Gall and Mallory[3]) or a reticulum-cell sarcoma (Jackson and Parker[12]), depending upon the classification followed. It is of interest that in view of the very undifferentiated and immature character of the lesion, this patient is still alive and well without evidence of recurrence, five and one-half years following resection.

The majority of the reported cases in the literature would seem to fall in the lymphocytic-cell type judging from what can be learned from the photomicrographs and cytologic descriptions. However, the cases reported by Maier,[6] Spatt and Grayzel,[5] and Grimes, Weirich, and Stephens[11] are more suggestive of lymphoblastoma types.

Case 1, in which only partial resection was done, was histologically the most bizarre and anaplastic lesion of the series. The sections were exceedingly pleomorphic with odd-sized and -shaped cells and numerous multinucleated giant cells. Frequent mitoses were evident as well as moderate polymorphonuclear cells, especially eosinophils. Necrosis and scattered fibrillar areas could be seen. Although the first diagnosis was undifferentiated epithelial cancer, review of this material resulted in its classification as Hodgkin's sarcoma. Figs. 3 and 4 are sections from this patient, the latter specimen being from the autopsy eight and one-half years following thoracotomy. At this time pronounced, dense collagenous tissue was apparent but still discernible were islets of bizarre, pleomorphic cells, some of which were very dark staining, indicating beginning necrotic changes. The appearance of the latter section was very similar to the long-standing, chronic "burnt-out" Hodgkin's disease. The long duration of this patient's illness is not in keeping with the generally known prognosis of the Hodgkin's sarcoma group.

Last, the pathologic features of the pleural fluid group were of interest in that cytologic examination of the blocked centrifuged fluid contained myriads of rather mature lymphocytes. Material obtained for histologic study in 2 of these patients at the time of thoracotomy was histologically identical with the lymphocytic type lymphosarcoma described previously. In one of these patients, the procedure was done to drain an empyema pocket and a section of the thickened pleural tissues revealed a pyogenic cellular reaction on one surface of the dense hyalinized tissue and on the other a very dense, cellular lymphosarcomatous infiltration (Fig. 18).

Two patients in this group had lymphocytic infiltration into the pleural fluid and had a final diagnosis of Hodgkin's disease. In 1, thoracotomy was done and revealed slightly enlarged lymph nodes in the inferior pulmonary

ligament and a single node superior to the azygos vein. Histologically, these were consistent with Hodgkin's disease, demonstrating pleomorphic cellular aggregates, eosinophilic polymorphonuclear leukocytes, and Sternberg-Reed cells. Although the other case did not have thoracotomy, the diagnosis of Hodgkin's disease was made from inguinal node biopsy. Very interestingly, this patient also had the typical lymphosarcoma infiltration which showed in a bronchoscopic biopsy. It is difficult to explain this, as the constancy of the lymphoma lesions is well shown in the figures of Gall and Mallory. About the only change occurring in individual cases was in degree of differentiation and that in only some 23 per cent. It might be possible to explain the bronchial infiltration as a very early stage in which the lymphocytic infiltration was so marked as to obscure the other cellular components.

In 5 patients with parenchymal disease, lobectomy was performed in 3 and pneumonectomy in 2, accomplishing complete removal of the lesion in all 5 cases. The hilar lymph nodes removed along with the lobe or lung were all negative for tumor. One other patient in this group had only partial removal of the tumor because of the widespread involvement and was treated with x-ray and nitrogen mustard therapy (Hodgkin's sarcoma, Case 1). Of interest was the delay in the clearing of the left lung field following irradiation.

The other patient with partial resection was in the pleural fluid group. The surgery consisted of resection of the extrapleural masses in the right chest and decortication of the lower lobe for the complicating superimposed empyema. After the diagnosis was established, roentgen therapy was given over the right chest and the lesion in the left lung disappeared.

The treatment in the pleural fluid group consisted of aspiration, x-ray, and nitrogen mustard therapy. In 2 patients, drainage procedures were necessary because of complicating pyogenic infections and, in 1, biopsy material was obtained to substantiate the diagnosis of lymphoma. One patient had a peripheral node biopsy made for diagnosis, which was also done in 1 patient in the parenchymal group (Case 6).

The results obtained in this series are summarized in Tables I, II, and III, the latter consisting of the resected cases. Three of the 5 patients with total resection are alive, the length of time varying from one and one-third years up to five and one-half years. One has been lost to follow-up, and one survived three years before dying of cardiac failure.

Of the 2 cases with partial resection, 1 survived for more than eight years and the other is alive more than thirteen years from the date of the first x-rays revealing an abnormality, and almost seven years from the time the diagnosis was established by surgical exploration and removal of tumor.

Four of the patients with pleural fluid died in periods ranging from five months to five and one-half years. The patient with the shortest survival time (Case 12) died away from the hospital and autopsy material was not available. This was the only patient in the entire group in whom the only material obtained for the diagnosis was pleural fluid.

TABLE III. RESULTS OF RESECTION IN PULMONARY LYMPHOMA

PATIENT	SITE	HISTOLOGIC DIAGNOSIS	TREATMENT	RESULTS
M. W. 9-45	Left lung	Hodgkin's sarcoma	Subtotal resection; nitrogen mustard; roentgen	Dead; 8½ yr. survival
A. F. 3-47	Right lung	Small-cell lymphosarcoma	Right pneumonectomy	Dead; 3½ yr. survival
C. S. 1-49	Left lung	Small-cell lymphosarcoma	Left upper lobectomy	Lost to follow-up after 2 yr.
W. J. 11-49	Right lung	Small-cell lymphosarcoma	Right upper lobectomy	Alive 5½ yr.
I. W. 11-49	Right lung	Lymphoblastoma	Right pneumonectomy	Alive 5½ yr.
G. C. 12-53	Left lung	Small-cell lymphosarcoma	Left lower lobectomy	Alive 1½ yr.
C. D. 1942	Bilateral	Small-cell lymphosarcoma	Subtotal resection; nitrogen mustard; roentgen	Alive 13 yr.

SUMMARY AND CONCLUSIONS

Seven cases of pulmonary and 5 of pleural lymphomas are reported with special emphasis directed toward the pathologic aspects and comparison of these and the clinical features with previously reported material.

Pulmonary resection with complete removal of the disease was accomplished in 5 patients with survival in 2 of these being over five and one-half years and in 1, one and one-third years. One patient was lost to follow-up after two years and 1 died after three years from cardiac failure.

Partial resection established the diagnosis in 2 others allowing for adjunctive therapy and survival rates of eight and one-half years in 1 and thirteen years in the other.

The majority of the lesions were of the lymphocytic-type lymphosarcoma and this group of patients was more favorable for resection as well as having the best survival rates.

The prognosis of the lymphoma group as a whole would seem to be more favorable than that for pulmonary or pleural carcinoma.

REFERENCES

1. Rubin, E. H.: Diseases of the Chest With Emphasis on X-Ray Diagnosis, Philadelphia, 1947, W. B. Saunders Company.
2. Robbins, L. L.: Roentgenological Appearance of Parenchymal Involvement of the Lung by Malignant Lymphoma, Cancer **6**: 80, 1953.
3. Gall, E. A., and Mallory, T. B.: Malignant Lymphoma; Clinico-Pathologic Survey of 618 Cases, Am. J. Path. **18**: 381, 1942.
4. Churchill, E. D.: Malignant Lymphoma and Pulmonary Coccidioidomycosis; Clinic on Surgical Lesions of Lung With Consolidation, S. Clin. North America **27**: 1113-1120, 1947.
5. Spatt, S. D., and Grayzel, D. M.: Primary Lymphosarcoma; Case Report and Review of the Literature, Ann. Int. Med. **27**: 632-638, 1947.
6. Maier, H. C.: Primary Lymphosarcoma of Lung, J. THORACIC SURG. **17**: 841, 1948.
7. Anlyan, A. J., Lovingood, C. G., and Klassen, K. P.: Primary Lymphosarcoma of the Lung; Case, Surgery **27**: 559-563, 1950.
8. Beck, W. C., and Reganis, J. C.: Primary Lymphoma of the Lung; Review of Literature, Report of a Case and Addition of Eight Other Cases, J. THORACIC SURG. **22**: 323, 1951.
9. Weissman, I., and Christie, J. M.: Primary Lymphosarcoma of the Lung; Report of Case, A. M. A. Arch. Surg. **62**: 129-133, 1951.
10. Sarokhan, J., and Morrison, D. A.: Primary Lymphosarcoma of the Lung, Ann. Surg. **138**: 140-143, 1953.

11. Grimes, O. F., Weirich, W., and Stephens, H. B.: Primary Lymphosarcoma of the Lung; A Report of Two Cases, J. THORACIC SURG. 27: 378-383, 1954.
12. Jackson, H., Jr., and Parker, F., Jr.: Hodgkin's Disease and Allied Disorders, New York, 1947, Oxford University Press.

DISCUSSION

DR. HERBERT C. MAIER, New York, N. Y.—I should like to give a follow-up on a case of small-cell lymphosarcoma that was referred to, in which the patient was operated upon ten and one-half years ago when a pneumonectomy was performed. The patient at that time was 50 years of age and (slide) had extensive involvement of the left lung including the whole upper lobe and a part of the lower lobe by infiltration across an incomplete fissure. The lymph nodes were negative. The subsequent course was as follows:

(slide) An x-ray taken three years later showed a lesion in the other lung that responded readily to small doses of radiation. He remained well until 1951, having had the pneumonectomy in 1944. A small lesion then appeared in the paramediastinal region which, as the next slide shows, increased in size.

(slide) Again with small doses of radiation, the lesion disappeared within a short time.

(slide) This is a recent inspiration and expiration film; you see there is excellent ventilation of the remaining lung which was not interfered with by the relatively small doses of irradiation. The patient has no dyspnea at the age of 61 which I think is largely due to the excellent expansibility of the remaining lung. He has been entirely asymptomatic and, as a matter of fact, did not even have symptoms at the time he showed roentgen evidence of recurrence of the disease.

(slide) I show this next case for a different purpose. This patient was operated on only three years ago for reticulum-cell lymphosarcoma. When this woman, who was in her 40's, came to us, she had x-rays that showed that the mass had almost doubled in size in a three-week period prior to operation. At operation, there was no lymph node involvement but just a large mass in the right middle lobe which involved the visceral pleura and had a granular appearance. The middle lobe was removed and she was well on a follow-up visit last week, three years after operation, in spite of the rapid growth of the neoplasm preoperatively.

DR. BRIAN BLADES, Washington, D. C.—Four cases of primary lymphosarcoma of the lung have been seen at the George Washington University Hospital. In these four cases there was one unique problem, which is probably worth describing.

The patient, a 40-year-old woman, had been using oily nose drops for many years. Her case had been used for demonstrations of lipoid granuloma for some time. She had bilateral x-ray changes compatible with this disease and fat droplets had been demonstrated in the sputum.

The internist in charge of her case had x-rays made at six-month intervals and, after a couple of years, noticed that on the right side the shadow was more opaque and was assuming a rounded, solid appearance. All her studies were repeated, but there was no clue as to what might be going on. Finally, it was decided to perform an exploratory thoracotomy. At that time a lymphosarcoma was found. No involved lymph nodes could be located in the mediastinum. Under ordinary circumstances, a pneumonectomy would have been performed, but there was a serious problem of contralateral disease, which also might be lymphosarcoma. We were reluctant, therefore, to remove the lung. Dr. Charles Thompson, the internist in charge of the case, made an excellent suggestion that we block off the side known to be involved with lymphosarcoma, with lead sheeting, and give x-ray therapy to the unknown or left side. After a test dose of x-ray there was no change in the left side, and we therefore proceeded with the pneumonectomy on the right. She is now alive and well after more than two years.

DR. ARTHUR H. AUFSES, New York, N. Y.—I think it is important to remember that in this disease there are some benign lesions. Had the essayist mentioned the first

4 cases in the literature I think he would have mentioned the 1 about which I am going to speak, which was published in the *Journal of the Mount Sinai Hospital* in 1951. This patient also had no pulmonary symptoms.

(slide) In 1947, she was found to have a lesion in the lung when she had gastrointestinal x-rays made because of some abdominal distress. The series was negative and the lesion was investigated. Two bronchoscopies were negative, and she was operated upon. A diffuse lesion was found in the upper lobe, infiltrating the middle and lower lobes. A pneumonectomy was performed because the pathologist thought this was a tumor on frozen section, although he could not say exactly what kind of neoplasm.

(slide) Here is a tomogram showing this mass; this was not atelectasis, this was tumor extending into the upper lobe. Our pathologist felt that this was what he would have to call a benign lymphoma; it was composed of a mass of mature lymphocytes which had replaced the pulmonary parenchyma and which had not invaded the bronchi or the arterial system. There were no mitoses. He could not call this lymphosarcoma as such. We decided not to give any further therapy to this patient. She is alive and well eight years after operation.

DR. JOHN F. HIGGINSON, Portland, Ore.—It is of interest to me that the authors found that bronchoscopy was of little diagnostic aid in these cases. My own experience has been very limited. In the *Journal of Thoracic Surgery* for December, 1950, Dr. Grismer and I reported an instance of obstructing intrabronchial Hodgkin's disease diagnosed by bronchoscopic biopsy. By way of follow-up report it might be interesting for the audience to know that this patient died May 31, 1953, of the disease. There was no autopsy. This was two months short of four years following diagnosis and x-ray therapy. He had been last seen with a negative bronchoscopy on July 18, 1950, twelve months following the original diagnostic bronchoscopy.

DR. JOHN L. POOL, New York, N. Y.—There are two points to which I should like to call attention. The first concerns diagnosis. We are all sure in our minds in this group, certainly, that any intrathoracic shadow, the nature of which is not clear, deserves diagnosis by histologic methods.

(slide) I would like to point out that in these shadows in the chest one should also consider the fact that a supraclavicular lymph node, even though not palpable, may furnish the diagnosis. I raise that question because of a second point, which is the question of primary treatment for lymphoma disease of the lung when diagnosis has been established. If there is no diagnosis possible by extrathoracic biopsy and intrathoracic biopsy is undertaken, it is my feeling that a minimal dissection of lung tissue is in order, because from the therapeutic point of view, radiation therapy is the treatment of primary choice. For instance, in a woman of 31 years of age, chest x-ray showed a 6 cm. spherical shadow in the anterior segment of the right upper lobe. A supraclavicular node was biopsied and showed Hodgkin's disease. Radiation therapy was employed to the neck and the localized pulmonary shadow and this slide shows the situation three years later with minimal scarring in that area, because radiation was kept to the local area. But, as also illustrated by other cases today, a new area appeared in the other lung which also disappeared under radiation therapy as the final slide shows. You see minimal scarring in both lungs and both areas are clear two years later. The conclusion is that intrathoracic surgery for the lymphomatous diseases is for diagnosis and that therapy by radiation methods is best.

DR. GEORGE W. B. STARKEY, Boston, Mass.—I would like to commend the authors for their interesting paper and briefly add 7 cases of intrapulmonary lymphomas which we (Starkey, Strieder, Lynch) gathered together recently. I agree with the authors that often supraclavicular node, pleural fluid, and bronchoscopic biopsy may fail to make the proper diagnosis and so thoracotomy should be done. This was necessary in our 7 cases.

Briefly, we had 4 cases of small-cell lymphosarcoma. Two of these patients merely had biopsies and died about nine and ten months, respectively, after biopsy. The other 2 had resections, 1 being alive and well four years postoperatively and the other alive and

well seven years later. The fifth had a reticulum-cell sarcoma, had a pulmonary biopsy, and was treated with nitrogen mustard, and is alive and well six and one-half years later. The sixth and seventh patients had Hodgkin's disease. One had a right upper lobectomy plus nitrogen mustard and x-ray and continues to do well after two years. The last patient merely had a lung biopsy and was treated with nitrogen mustard and x-ray and is also well more than two years later.

DR. JOHN M. SNYDER, Bethlehem, Pa.—I would like to add one more case which presented several interesting points. The patient, a 35-year-old woman, the mother of three children, presented herself in March, 1952, because of hemoptysis and upper retrosternal pain of one and one-half months' duration. Physical examination was negative, and x-ray of the chest showed a left upper hilar mass which in lateral view appeared slightly anterior and superior to the hilum. Bronchoscopy was grossly negative, but washings of the upper lobe bronchus were reported as showing small collections of cells resembling lymphocytes, variable in size and hyperplastic in appearance, suggesting the mass to be a lymphoma in the lung.

At exploration, the mass was found to be primarily in the upper lobe, and later pathologic examination showed it to arise in one of the primary apical divisions of the left upper lobe bronchus leading directly into the area. At the operating table what was considered to be a direct extension into the mediastinum involved the apex of the pericardium at the anterior base of the aorta, and after resection of this part of the pericardium, the mass was found also to involve the left lateral wall of the superior vena cava. The lateral wall was resected for about 1½ inches, and since a frozen section at the time from a single contiguous mass was misinterpreted as a carcinoma, a left pneumonectomy was performed. No superior vena caval compression syndrome resulted as quite an adequate amount of vein had been left. Fixed section examination of the lung mass, approximately 5 by 4 by 3 cm. in size, showed it to be a Hodgkin's granuloma. The mediastinal extension on cut section showed several matted nodes. The edges of the pericardium and superior vena cava removed with the mass were microscopically tumor free.

The patient received 2,500 r of x-ray therapy postoperatively, and as the x-ray shows is alive and well without evidence of recurrence or metastasis three years later.

DR. ROBERT J. JENSIK (Closing).—I would like to thank the discussers for their remarks, and for the addition of the cases they have seen. I am interested in what Dr. Maier said about the result in his patient. A lot can be learned by comparing end results with the histologic types of lymphomas, although there is no absolute correlation seen. In one of our cases the picture was that of a very immature lymphocytic lymphoma, and the survival was more than five and one-half years which is an exception. Our first case was Hodgkin's sarcoma and the survival of more than eight and one-half years was not in keeping with the prognosis in Hodgkin's sarcoma. So that all we can do is offer generalities which will bear support as additional material is collected.

With regard to Dr. Aufses' reference, we did not quote that, but I would like to say that making the diagnosis of benign lymphoma should be done with the fingers crossed. Several of the patients in our series had a histologic picture of very mature lymphocytes in keeping with the picture of mature lymphoid tissue. One patient of this group had disseminated lesions to the lymph nodes of the neck, inguinal region, and opposite lung at the time of death.

With regard to Dr. Pool's remarks, we always examine for peripheral nodes, because the demonstration of tumor in these in many cases precludes resection of the chest lesion. In none of the patients of this group in whom complete removal of the tumor was accomplished was peripheral lymph node involvement found. Furthermore, the hilar lymph nodes were free of any changes suggestive of lymphoma.

PROSTHESIS FOLLOWING EXCISION OF CHEST WALL TUMORS

BERT H. COTTON, M.D., GEORGE A. PAULSEN, M.D. (BY INVITATION), AND
JACK DYKES, M.D. (BY INVITATION)
LOS ANGELES, CALIF.

SURGICAL management of 20 patients with chest wall tumors is reviewed. Criteria for chest wall prosthesis are proposed and critical areas in which replacement problems may be encountered are discussed. Stainless steel ribs or struts with fine malleable steel mesh proved to be the prosthesis of choice. Present results with this method are encouraging.

Ideal surgical treatment of chest wall tumor must accomplish two objectives: adequate excision, and return of the physiology as nearly as possible to normal. For 60 years surgeons have successfully removed large segments of the chest wall. For an equal period of time, they have been less successful in restoring normal chest wall function. The obstacles encountered are, first, the wide deforming defect; and second, the seriously altered pulmonary physiology.

A wide variety of prostheses, or none at all, will prove adequate for small defects of the chest wall. Hence the critical test of any reconstructive method is its adaptability to large defects. If successful prosthesis is to be achieved in such instances, the following criteria must be fulfilled: The unsightly deformity must be eliminated. A chest wall must be provided which is strong enough to resist blows that might injure underlying structures. This chest wall must be sufficiently rigid to prevent paradoxical motion and impaired cough mechanism and to support overlying heavy bone and muscle structures, particularly the weight of the scapula; yet it must be flexible enough to allow physiologic chest wall movements to institute proper alveolar gaseous exchange. Pain should not exceed usual expectations. Minimal bacterial contamination at operation is, of course, a requirement.

EVOLUTION OF CHEST WALL PROSTHESIS

Radical resection of chest wall tumors was recorded early in the literature. Even before 1894,[1] wide block resection of the chest wall with segments of the involved lung had been successfully performed. Although some authors[2-6] considered that repair of the defects was not essential, most surgeons have attempted reconstruction since 1894 when Volger[7] suggested the use of osteoperiosteal flaps.[8-10, 22] The first materials employed for this purpose consisted of adjacent tissue—periosteum, muscle,[11, 12] thoracic and abdominal soft tissue flaps, including the female breast,[13-15] with skin grafting if necessary. Successful results with fascia lata grafts in large sheets or woven strips have been re-

Read at the Thirty-fifth Annual Meeting of The American Association for Thoracic Surgery at Atlantic City, N. J., April 24 to 26, 1955.

TABLE I

NAME	AGE	SEX	OPERATION	PATHOLOGY	DATE OF OPERATION	TYPE OF PROSTHESIS*	ALIVE OR DEAD† (YEARS)	PREVIOUS SURGERY
J. F.	32	M	Sternum, gladiolus, and xyphoid	Reticulum-cell sarcoma of sternum	1-12-48	Tantalum plate	Dead (2)	0
M. M.	60	F	6 through 8	Adenocarcinoma of lung	6- 6-49	Mesh No. 46	Dead (1)	0
S. B.	34	F	2 through 4	Recurrent adenocarcinoma of breast	8-22-49	Mesh No. 46	Working	Mastectomy and recurrence with wide ulceration
W. M.	54	M	Lat. ½ of 2 through 6	Sarcoma mesothelioma	12- 1-50	Mesh No. 46	Dead (1)	0
F. D.	70	M	Ant. ½ of 7 and 8 and rt. pneumonectomy	Squamous-cell carcinoma	2-19-51	Mesh No. 46	Dead (1)	0
M. S.	75	M	Ant. ½ of 2 through 4	Fibromyxoma	3- 5-51	Mesh No. 46	Working	0
L. D.	48	F	Ant. ½ of 3 through 6	Adenocarcinoma of breast	11- 2-51	Mesh No. 46	Working	Bilateral mastectomy and recurrence with ulceration
O. S.	49	M	Lat. ½ of 5 and 6 plus pneumonectomy	Squamous-cell carcinoma	3-20-52	Mesh No. 46	Dead (1)	0
M. S.	16	F	Post. seg. 8 and 9	Giant-cell tumor	9- 4-52	Mesh No. 40	Working	0
M. M.	60	F	Sternum and rt. ant. 2 through 4	Adenocarcinoma	10- 6-52	Mesh No. 20	Working	Mastectomy and recurrence with ulceration
D. B.	46	F	Ant. to post. 2 through 7	Reticulum-cell sarcoma	11-17-52	Mesh No. 20	Dead (2)	0
L. M.	62	M	Ant. to post. 1 through 3 plus RUL	Adenocarcinoma	2- 6-53	Mesh No. 46	Dead (1)	0
B. V.	46	F	Diaphragm and lat. ½ of 9 and 10	Mesothelioma	4-13-53	Mesh No. 46 for diaphragm and chest wall	Dead (2)	0

J. R.	48	M	6 through 11, LLL, Diaphragm and spleen	Osteochondroma	12- 2-53	Mesh No. 20 with steel rib and polyethylene diaphragm	Working	3 attempts	
J. C.	68	M	Ant. ⅔ of 6 and 7	Fibrous dysplasia	2-22-54	Mesh No. 40 and steel rib	Working		0
C. B.	33	M	Lat. ½ of 5 through 9	Round-cell sarcoma	4-12-54	Mesh No. 40 and steel rib			1
			Thoracotomy	Extensive recurrence	9-27-54	Mesh No. 20 and steel rib	Dead (1)		
O. S.	19	M	2 through 5 and RUL	Reticulum-cell sarcoma	6- 4-54	Mesh No. 40 and steel ribs	Working		0
R. H.	68	M	Ant. and lat. ⅔ of 6 through 10 and rt. pneumonectomy	Fibrosarcoma					
L. B.	60	F		Neurofibroma	12- 1-39			Excision of neurofibroma	
				Sarcoma	10-11-48			Excision of local sarcoma with segmental lobectomy	
			Post. and lat. ⅔ of 5 through 11 and lobectomy	Fibrosarcoma	9- 9-54	Mesh No. 40 and steel ribs	Working		
D. W.	58	F	Ant. ½ of 4 through 10	Myxosarcoma	2- 4-52	Mesh No. 20	Working	2 attempts	
			Post. ½ of 4 through 10		1-13-55	Mesh No. 40 and steel rib			

*United Foundation wire mesh.
†Survival rate over 6 months listed as 1 year.

ported.[16-18] Later, repair of chest wall defects was accomplished by means of adjacent ribs either split or divided in such a way that they could be pulled down over the defect. Tibial grafts,[19] or rib and cartilage in strut or diced form were employed also.

In 1909,[20] metallic prosthesis was proposed. Tantalum plates[13, 17, 21-27] were the first metallic replacements used in the chest but were largely unsuccessful[17, 22-27] because of complicating hemorrhages and infections. Regardless of the substance used and even in the absence of tissue reaction, it appears unlikely that a fixed plate could become an integral part of the supporting tissues of the chest wall. A smooth plate resists intimacy with surrounding tissue. When the involved structures are subject to constant changes in stress the possibility of union is still more remote.[22, 23, 28] Tantalum mesh has been used with success to repair chest wall defects as well as in other parts of the body.[8, 28-31] In a recently reported series of cases,[28] however, a change from this material to stainless steel wire was made after late fragmentation of the tantalum mesh occurred. Owing to excessive tension, 2 patients sustained local skin necrosis which produced separation of the wound down to the mesh. The necrotic area healed by granulation without sinus formation.

AUTHORS' SERIES

Statistical data concerning the 20 cases comprising the present series are summarized in Table I. Three patients with benign tumors are alive and well an average of 3 years and 6 months after operation. Of 10 patients with

TABLE II. CHEST WALL TUMORS

	ALIVE		DEAD	
	NO. CASES	AVERAGE YEARS OF SURVIVAL	NO. CASES	AVERAGE YEARS OF SURVIVAL
Benign	3	3.6	0	
Malignant	5	3.3	5	1.7
Metastatic	3	4.4	4	1.1

primary malignant tumors of the chest wall, 5 are alive an average of 3 years and 3 months after operation while 5 died an average of 1 year and 7 months postoperatively. Metastatic extensions of breast carcinoma were present in 3 patients, all of whom are well an average of 4 years and 4 months after surgery. Four patients with metastatic extensions of lung tumors died an average of 13 months postoperatively. There were no deaths 6 months after operation in this series.

TABLE III. TYPE PROSTHESIS

Tantalum plate	1 case
Steel mesh	13 cases
Steel mesh with steel rib	6 cases

Insofar as possible, excision and prosthesis for chest wall tumor should be considered separately; otherwise, a compromise resection of the tumor may result.

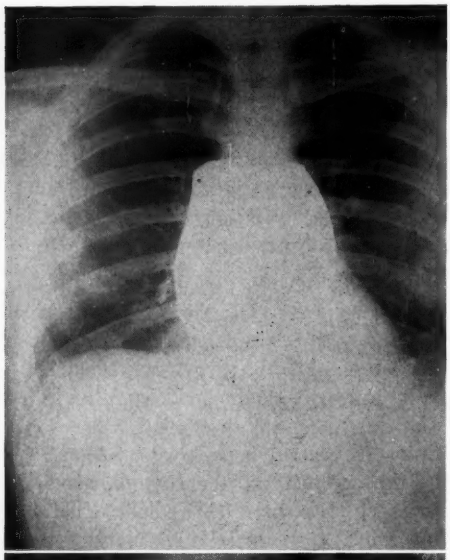
Resection.—Adequate resection requires excision of the tumor and involved rib or ribs together with a safe margin of adjacent tissue. In our series this margin included 3-inch segments[32, 33] of ribs beyond the tumor. Intramedullary extension may occur as far as 3 inches into the involved bone. Furthermore, microscopic nodules of the tumor have been found in distant periosteum and recurrence in the rib stumps has not been uncommon. The margin should include intercostal muscles above and below, a procedure executed with minimal danger of transecting tumor nodules by removing segments of adjacent ribs, underlying parietal pleura with lung tissue if involved, and immediate overlying skeletal muscle with skin, if involved, en bloc. This type of resection is a minimum for malignant tumors.[17, 34, 35] Other structures may be included as indicated.

Prosthesis.—An arbitrary indication for prosthesis is the removal of two or more long rib segments. Re-establishment of chest continuity should then be attempted in accordance with the previously mentioned criteria. Three areas exist in which it is most difficult to accomplish effective stabilization. The first critical area is the anterior chest wall where lack of overlying soft tissue and wide interspaces present a problem. Second, resections extensive enough to undermine the supports of the scapula necessitate a replacement that will support the heavy structures of the back. Third, if the excision extends through the lower intercostal margins, a substitute must be envisioned to maintain support for the lower border of the chest wall, pull of the diaphragm and the liver or stomach.

Our experience began in 1948 with an operation for a reticulum-cell carcinoma of the sternum. A longitudinal incision was made over the lower border of the chest and a skin flap dissected upward so that the line of incision would not be over the prosthesis. The surgical excision required removal of a portion of the manubrium, the entire gladiolus, ziphoid process, and segments of the cartilaginous ribs on both sides of the sternum. A large tantalum plate was fitted to the defect and sutured in place with tantalum sutures. The plate previously had been drilled with many perforating holes so that it could become firmly anchored by tissue growth. Entrance into the right pleural space was made during the procedure. The pneumothorax was effectively controlled postoperatively by an intrapleural catheter. Postoperative results in this instance were satisfactory. The plate became firmly fixed and the wound healed per primam. Excellent protection to the anterior mediastinum was achieved. Success was credited to the many perforations in the tantalum plate which rapidly became solidly anchored in the tissue.

This type of replacement, although it may still be considered applicable for the sternum, presents certain disadvantages. The tantalum plate proved difficult to mold to the sternal defect and would be much more difficult to mold to the curvature of the ribs. Moreover, the material is unnecessarily heavy. Because of favorable reports in the literature and our own experience with stainless steel suture material over tantalum, we decided to try stainless steel mesh in subsequent cases. On June 6, 1949, the stainless steel mesh was first

Fig. 1.



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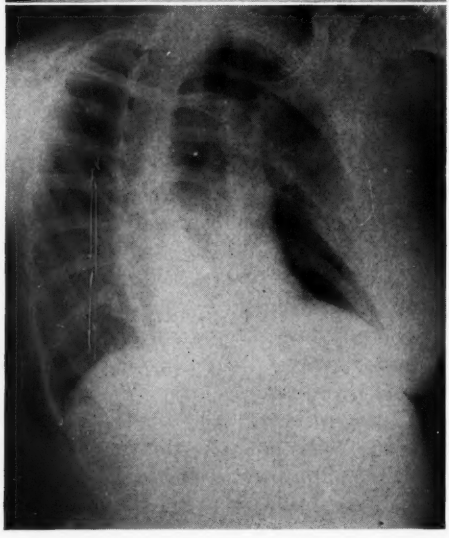

Fig. 1.—J. F. Tantalum plate replacing sternum. Close scrutiny shows holes bored through plate which aided fixation of the prosthesis.

Fig. 2.—D. B. Preoperative view of sarcoma on right posterolateral chest which has eroded right fifth rib and portions of the fourth and sixth ribs.

Fig. 3.—D. B. Same patient postoperatively displaying buckled plate of unsupported mesh.

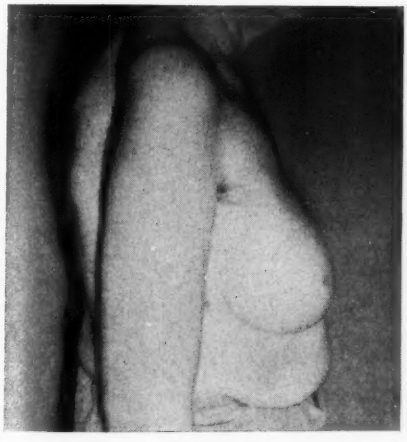

Fig. 4.

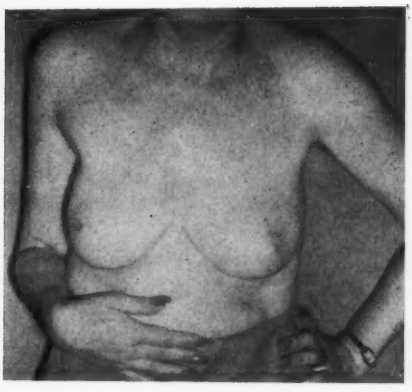

Fig. 5.

Fig. 4.—D. B. Lateral view showing sunken right chest wall due to scapula weight on steel mesh inadequate for supporting shoulder weight.

Fig. 5.—D. B. Anterior view showing fixed right scapula. Shoulder weight too great for unsupported mesh. Anteriorly with no weight to buckled prosthesis shows no deformity.

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Fig. 6.

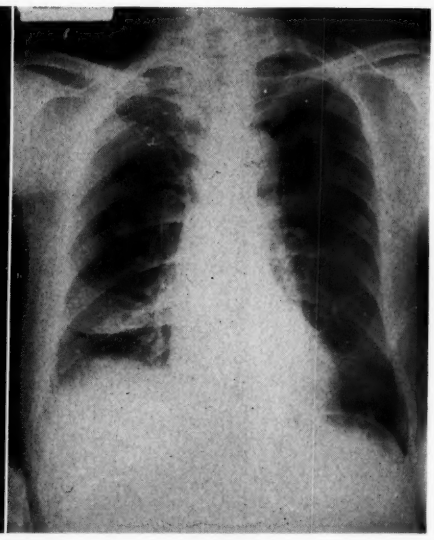


Fig. 7.

Fig. 6.—M. S. Preoperative film (of soft tissue technique) showing tumor on anterior chest.

Fig. 7.—M. S. Same patient with prosthesis of stainless steel mesh replacing portion of right anterior chest wall.

Fig. 8.—D. W. Example of deformity from depressed chest wall. This patient had an infection of space about prosthesis requiring removal of the heavy mesh.

employed following a right pneumonectomy for adenocarcinoma. A block resection of the posterior chest wall was necessary to remove the lung. Segments of the sixth, seventh, and eighth ribs were excised. A single sheet of No. 46 mesh was used successfully. This material was later employed on several occasions and appeared to provide adequate reinforcement of the chest wall.

On March 5, 1951, we first experienced difficulty with stainless steel mesh following a large block resection of the anterior chest wall which included the second, third, and fourth ribs. The support proved too weak to form a rigid replacement for such a large defect. Limited paradoxical motion occurred with depression of the replacement toward the lung, causing the edges of the overlapping mesh to exert some pressure on the skin. The result was adequate but not ideal. Even today the area demonstrates mobility when the patient coughs.

In order to lend added strength to the prosthesis, we adopted a heavy-weight stainless steel screen wire, No. 20 in subsequent cases. This regulation screen wire proved very satisfactory for several large anterior defects and probably would have served as well as the tantalum plate in resections of the sternum. In the remaining two critical areas, however, it was unsatisfactory. Following an excision block including the inferior costal margin, the screen wire was molded to the curve of the ribs where it was sutured because of its springlike tendency. The sutures broke whereupon the unanchored edge sprang out causing so much pressure pain and skin deformity that its removal was necessary. The heavy-weight screen wire has no resilience. It further proved unsatisfactory for the critical subscapular area where a large sheet was used following an extensive chest wall dissection of the entire second, third, fourth, fifth, and sixth ribs with the lateral half of the seventh which undermined the support of the scapula and heavy back muscles. Despite the heaviness of the mesh No. 20 and the outward arch which added to its strength, the posterior portion buckled and allowed the scapula to be displaced inward, causing a severe posterior deformity. Another disadvantage of the heavy mesh support is its size and weight; in this respect it is similar to tantalum plates, a slow resisting intimacy of the surrounding tissue. Thus, immediate postoperative infection will always require removal of the prosthesis. No such problem was encountered in reported cases in which fine mesh was employed.[28]

Our next attempt to design a satisfactory prosthesis concerned a recurrent chondroma weighing 22 pounds which occupied the entire lower half of the left chest and necessitated removal of the sixth, seventh, eighth, ninth, tenth, and eleventh ribs, left lower lobe, spleen, left diaphragm, and the greater portion of the lumbar muscles. A special prosthesis was made from heavy stainless steel mesh with supporting stainless steel ribs. Unfortunately, this did not fit the defect perfectly and was extremely awkward to refashion at the operating table. Because of extensive skin flaps, heavy weight of prosthesis, and tension of the suture line, necrosis occurred, uncovering the mesh. Widespread infection required removal of the prosthesis.

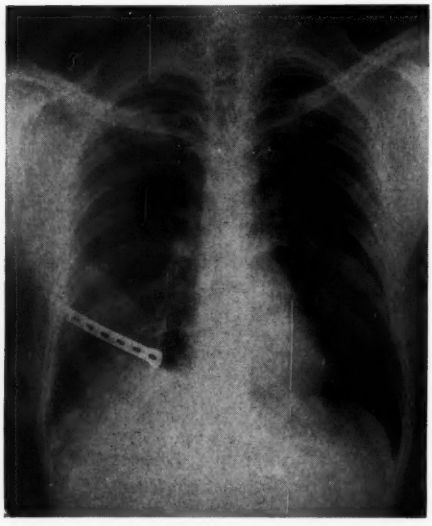


Fig. 9.—C. B. One strut support for mesh prosthesis.

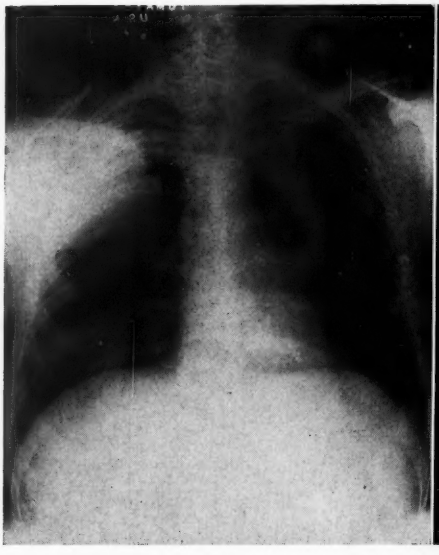


Fig. 10. Fig. 11.

Fig. 10.—O. S. Preoperative view of right chest wall tumor which has dissolved lateral portion of right third rib.

Fig. 11.—O. S. Prosthesis of two-rib strut support to fine mesh which was fashioned at operating table to tailored size.

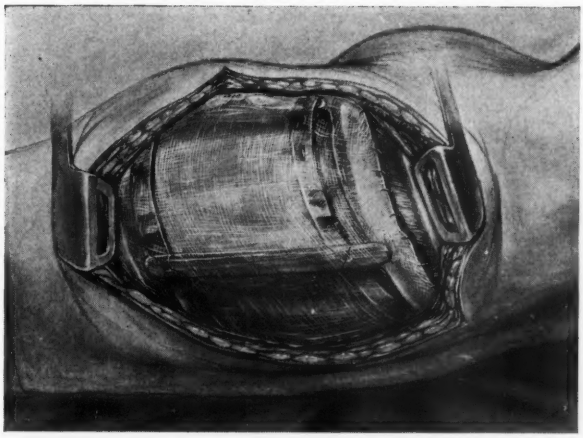


Fig. 12.—Strut prosthesis in place showing malleable mesh supported by stainless steel rib supports.

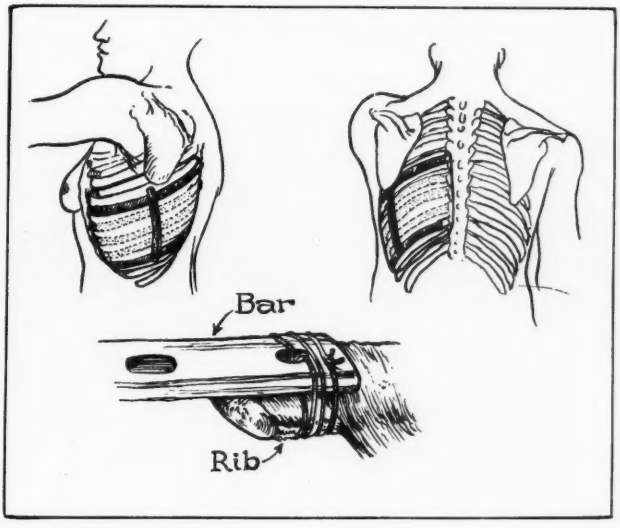


Fig. 13.—This view shows method of attachment of strut to adjacent normal rib end. It also shows lack of deformity.

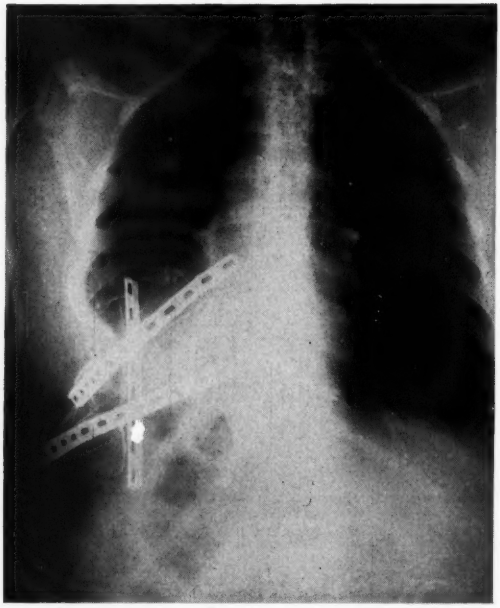
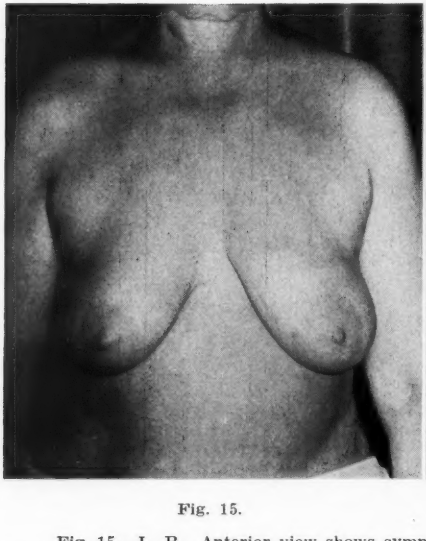


Fig. 14.—L. B. Three-rib strut support to fine malleable mesh with one-rib strut as cross strut.



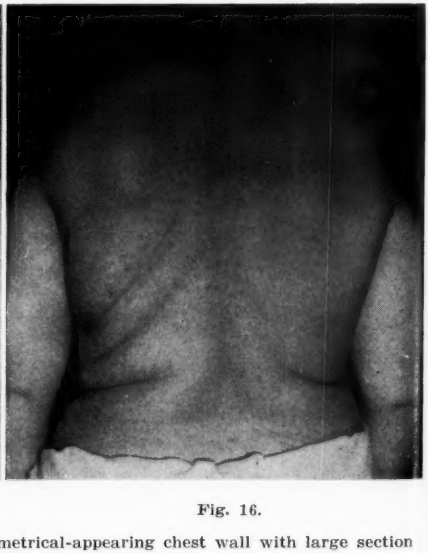


Fig. 15. Fig. 16.

Fig. 15.—L. B. Anterior view shows symmetrical-appearing chest wall with large section replaced by prosthesis described.

Fig. 16.—L. B. Posterior view of same patient.

The present method, evolved from our experience with chest wall replacements, consists of stainless steel rib struts, about one for every two ribs removed, placed strategically over the defect and anchored to the posterior and anterior portions of the ribs. A perpendicular cross strut may be used to provide additional strength. This scaffold will perform the weighty duties of the thorax. A fine malleable mesh placed over or under the frame of the strut acts as matrix and lattice for tissue growth and performs the less strenuous task of resisting intrapleural pressure changes. Such a pattern allows the surgeon considerable leeway for construction at the time of operation owing to the various lengths of orthopedic bone plates available as struts and the malleability of the fine steel mesh which is integrated into the tissue rapidly with no pressure points. We have encountered no complications with this type of prosthesis and postoperative results have been satisfactory. As compared with previous techniques, we feel our present method more fully meets the criteria for a successful prosthesis. It more nearly duplicates the normal anatomy of the chest wall and provides a better physiologic functional chest with adequate mobility but with sufficient rigidity for support. By clinical application, we have established that this type of prosthesis will meet the demand for scapula posteriorly, will effectively stabilize the chest anteriorly, and will substitute for a lower costal border; that is, it serves satisfactorily in the three critical areas previously defined. It may be used effectively to stabilize the lower costal edge after resections of the lower chest extending through the inferior costal border to the abdominal muscle wall. If the attachment of the diaphragm must be dissected, it may be reattached through the screen to the underlying muscle or skin tissue adjacent to one of the supporting steel struts. Diaphragmatic action thus is not lost. The prosthesis therefore meets the critical test of adaptability to large chest wall defects, including those in which stabilization is most difficult to accomplish by other methods.

COMPLICATIONS

The complication encountered in this series was infection, occurring in 2 patients both of whom had prostheses made of heavy mesh. In one of these patients the skin necrosed at the incision line owing to extensive skin flaps and tension of suture line. Heavy prosthesis was considered the cause. Contrary to reported observation in patients in whom fine mesh was employed,[28] a widespread infection was encountered as soon as the screen became visible. This may be related to the lesser facility with which the heavy screen wire is incorporated in the tissues. The second instance of infection occurred after an extensive chest resection including ribs four, five, six, seven, eight, nine, and ten, accompanying a lower lobectomy. A temporary bronchopleural fistula was the origin of infection. In both cases it was necessary to remove the prosthesis in order to control the infection and then to make a fresh start toward eliminating the defect.

SUMMARY

1. The results of excision and prosthesis in 20 cases of chest wall tumor are presented.

2. Criteria for the prosthesis are suggested and critical areas which may prove difficult to manage satisfactorily are pointed out.

3. A new type of prosthesis is proposed which appears to fulfill essential criteria. The replacement, consisting of stainless steel ribs with fine malleable steel mesh, proved satisfactory in critical areas in the patients to whom it was applied.

4. The final test of a prosthesis is its adaptability to large defects. A variety of replacements or none at all will be satisfactory for smaller defects.

The authors wish to express their thanks and appreciation to Mrs. Helen Gindy, Librarian of the Huntington Memorial Hospital, Pasadena, Calif.

REFERENCES

1. Paget, S.: Surgery of the Chest, New York, 1897, E. B. Treat & Co.
2. Richardson, W. G.: Enchondroma of the Manubrium Sterni Successfully Removed by Operation, Brit. M. J. **1**: 985-986, 1913.
3. Hauer, G. J.: Thoracic Tumors, Arch. Surg. **18**: 271-282, 1929.
4. Graham, E. A., Singer, J. J., and Ballon, H. C.: Surgical Diseases of the Chest, Philadelphia, 1935, Lea & Febiger.
5. Head, J. R.: Discussion of papers by Harper and by Janes, J. THORACIC SURG. **9**: 161, 1939.
6. Bradshaw, H. H., and Chodoff, R. J.: Chondrosarcoma of the Sternum, Am. J. Surg. **48**: 685-687, 1940.
7. Volger, M.: Beitrag sur Kenntniss der Traumatischen Lungeon-hernien, Monatsschr. Unfallheilk., Leipz. **5**: 169-176, 1898 (Quoted from Ada, A. E. W., and Hevenor, E. P.[8]).
8. Ada, A. E. W., and Hevenor, E. P.: Reconstruction of Defects of the Thoracic Wall With Tantalum Mesh Gauze, J. THORACIC SURG. **21**: 125-134, 1951.
9. Goodman, H. I.: Hernia of the Lung, J. THORACIC SURG. **2**: 368-379, 1933.
10. Montgomery, J. G., and Lutz, H.: Hernia of the Lung, Ann. Surg. **82**: 220-231, 1925.
11. Campbell, D. A.: Reconstruction of the Anterior Thoracic Wall, J. THORACIC SURG. **19**: 456-461, 1950.
12. MacManus, J. E., McCormick, R. C., and Fechner, M. P.: Problems in the Management of Anterior Chest Wall Tumors, Surgery **34**: 245-253, 1953.
13. Maier, H.: Surgical Management of Large Defects of Thoracic Wall, Surgery **22**: 169-178, 1947.
14. Pickrell, K. L., Baker, H. M., and Collins, J. P.: Reconstructive Surgery of Chest Wall, Surg., Gynec. & Obst. **84**: 465-476, 1947.
15. Pickrell, K. L., Kelley, J. W., and Marzoni, F. A.: Surgical Treatment of Recurrent Carcinoma of Breast and Chest Wall, Plast. & Reconstruct. Surg. **3**: 156-172, 1948.
16. Mayer, L.: Chondrosarcoma of Rib, Bull. Mt. Sinai Hosp. **7**: 467-470, 1941.
17. Watson, W. L., and James, A. G.: Fascia Lata Grafts for Chest Wall Defects, J. THORACIC SURG. **16**: 399-406, 1947.
18. Winkel, A. H.: Hernia of the Lung, J. THORACIC SURG. **4**: 627-634, 1935.
19. Kinsella, T. J., White, S. M., and Koucky, R. W.: Two Unusual Tumors of the Sternum, J. THORACIC SURG. **16**: 640-667, 1947.
20. Gangolphe, M., and Tixier, L.: Enorme enchondrome de la fourchette sternale, Lyon Chirurg. **2**: 112-117, 1909.
21. Hedblom, C. A.: Tumors of Bony Chest Wall; Study of 22 Personal and 78 Collective Cases Since 1921, Ann. Surg. **98**: 528-545, 1933.
22. Maurer, E., and Blades, B.: Hernia of Lung, J. THORACIC SURG. **15**: 77-98, 1946.
23. Effler, D. B., and Blades, B. B.: Function of Thoracic Surgery Centers in World War II, Am. J. Surg. **72**: 319-330, 1946.
24. Griswold, R. A.: Osteochondrosarcoma of Sternum; Use of Tantalum as Prosthesis, Arch. Surg. **55**: 681-688, 1947.
25. Campbell, D. A.: Resection of the Sternum for Metastatic Carcinoma, Ann. Surg. **129**: 394-398, 1949.
26. Beardsley, J. M.: The use of Tantalum Plate When Resecting Large Areas of the Chest Wall, J. THORACIC SURG. **19**: 444-455, 1950.
27. Paulson, D.: Cited by Maurer and Blades.[22]
28. Effler, D. B.: Prevention of Chest Wall Defects, J. THORACIC SURG. **26**: 419-426, 1953.
29. Shefts, L. M.: Discussion of paper by Effler.[28]
30. Alexander, E. W.: Discussion of paper by Effler.[28]

31. Mendelsohn, H. J.: Discussion of paper by Effler.[28]
32. Upshaw, J. E., McDonald, J. R., and Ghormley, R. K.: Extension of Primary Neoplasms of the Bone to Bone Marrow, Surg., Gynec. & Obst. **89**: 704-714, 1949.
33. Halpert, B., and Davis, J. B.: Chondrosarcoma; Report of Two Cases, Am. J. Cancer **23**: 784-790, 1935.
34. Janes, R. M.: Primary Tumors of Ribs, J. THORACIC SURG. **9**: 145-159, 1939.
35. O'Neal, L. W., and Ackerman, L. V.: Cartilaginous Tumors of Ribs and Sternum, J. THORACIC SURG. **21**: 71-106, 1951.

DISCUSSION

DR. RALPH A. DETERLING, Jr., New York, N. Y.—I have been interested in chest wall replacement for several years because of the occasional patient with respiratory obstruction from pressure by an aortic aneurysm. We usually "floated" the manubrium by resecting the adjacent attachments, but did work on Lucite replacements in the laboratory. This could be molded to shape with heat, and it was well tolerated in dogs.

We have also used a taffeta fabric of synthetic material in patients to fill defects of the chest wall. It is easily cut to shape and, if sewn under some tension, the patch renders support. The ingrowth of fibroblasts soon stiffens the material. Should contour be desired, one can use the twelfth rib of the patient or homografts from the bone bank. I think the results mentioned by the authors are commendable, and present these other methods only to show additional ways in which defects of the chest wall may be handled.

THYMIC NEOPLASMS

DONALD B. EFFLER, M.D., AND LAWRENCE J. MCCORMACK, M.D. (BY INVITATION)
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INTRODUCTION

ALTHOUGH the thymus is present in most chordates, the function of this ductless gland is not understood and it presents an enigma that perplexes both the research investigator and the clinician. Interest in the thymus reached its peak in the early 1940's,[1] as clinicians sought to correlate myasthenia gravis with thymic dysfunction. Enthusiasm began to wane with the disappointing results of thymectomy for myasthenia; in fact, the related mortality and the poor results promoted an element of suspicion and surgical resistance to all diseases of the thymus. It is unfortunate that thymic tumors were contemplated more in the light of possible relation to myasthenia gravis than for their true property as mediastinal tumors of a high malignant potential. Thymic neoplasms occur more frequently than is commonly believed and are malignant in a high percentage of cases.

A review of the histopathologic features and the suggested classification are indeed bewildering. More important is the inability of the pathologist to distinguish between the tumor of the myasthenic and the asymptomatic patient, and also to differentiate between the cell of a benign thymoma and one that is highly malignant.[2-4, 8] The intriguing subject of thymic neoplasms requires new thought and clarification. To uncover the primary physiology of the thymus will require a great deal of basic research; in the meantime, these reports may be of value in pooling clinical information in cases of thymic disease. With the latter thought, the authors present a personal series of 19 cases.

CLINICAL FEATURES

Experience.—The patients in this series have been studied in the Department of Thoracic Surgery at the Cleveland Clinic. No case histories were removed from the archives of this or other institutions to increase the range of the series. This restriction was imposed in an effort to strengthen our ultimate conclusions.

A total of 26 cases of thymic neoplasms were accepted for consideration. After careful study, 7 of these were excluded; we believe this to be worthy of mention as this group of 7 included tumors that were intrathymic in locale, but whose cellular origin was in doubt. Such tumors of doubtful origin may have been included in other reported series and be responsible for considerable

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variation in thymic tumor classification. The 7 discarded cases include: 3 symptomatic hypertrophies that persisted following irradiation, 2 intrathymic dermoid cysts, and 2 anterior mediastinal seminomas.

The 19 cases (Table I) were selected on the basis of clinical and histopathologic study—adequate tissue having been obtained in each case. There is little doubt that undifferentiated bronchiogenic carcinoma and lymphosarcoma may be misdiagnosed as malignant thymoma; conversely a malignant thymoma may be mistaken for either of the entities just mentioned which closely resemble it. It is quite likely that older published series may contain examples of such understandable error; there is no reason to believe that this series or those of the future will be immune to similar error.

Myasthenia Gravis.—The association between thymic neoplasms and myasthenia gravis has been observed, but is not understood.[1, 5] Of the 19 patients in our series, 6 had or developed myasthenia gravis, and all 6 of these patients had tumors classified as malignant. This latter finding is significant as other writers have concluded that myasthenia gravis is seen rarely with a malignant neoplasm.[5-7] It is difficult to reconcile this divergency; perhaps the difference rests in the criteria of establishing malignancy in a thymic tumor.

From the standpoint of the myasthenia gravis, it appears that none of the 6 patients benefited by treatment of the neoplasm. One patient (Case 1, G. L. H.) did not develop symptoms of myasthenia gravis until 3 years after a highly malignant thymoma had been diagnosed and had been treated by radiation therapy; the patient died in an acute myasthenic crisis 3 days after a second operation had been performed for resection of the irradiated neoplasm. Another patient (Case 4, F. L.) had temporary relief from myasthenia gravis following removal of an apparently benign tumor. Three years later the patient died; the cause of death was attributed to tumor recurrence and severe myasthenia gravis. Only 1 patient with myasthenia gravis (Case 11, M. C.) in this series is alive. All of the others died, 4 with obvious metastases and with myasthenia gravis, and 1 other who suffered a fatal complication (aspiration pneumonitis) after a diagnostic curare test. Even though this group of patients is small, the factor of established malignancy in each of the 6 cases is important and contradicts the observations of Binkley,[7] Poer,[8] and others. Equally important is the observation that 4 of those patients succumbed to the cancer factor rather than to myasthenia gravis.

PATHOLOGY

Tumors of thymic origin demonstrate properties that make them unique among all mediastinal tumors. These tumors may be solid or cystic, well encapsulated, or extremely invasive, soft, or calcific. Thymic tumors may be wildly malignant, but limited in their scope of metastases. In the series of Binkley and associates,[7] 16 of 21 tumors were malignant, but none showed distant metastases. It is the caprice of the thymoma that has prompted us to consider all as malignant in fact or potential; it is this property that deserves the greatest emphasis and not the uncertain relationship with myasthenia gravis.

TABLE I.

CLINIC NUMBER	CLINICAL HISTORY	AGE	SEX	MYASTHENIA GRAVIS
1. 532-365 (G. L. H.)	Initial exam., 1947, normal; routine physical Feb., 1951—large mediastinal tumor; Aug., 1951, pain in right chest, x-ray showed intrapleural metastases right chest	34	F	Appeared late, 2½ years after biopsy of tumor
2. 580-560 (G. H.)	Calcified mediastinal tumor per routine x-ray June, 1949, no symptoms; in Nov., 1952, developed signs of severe congestive failure; x-ray showed tremendous cardiac silhouette	54	M	None
3. 563-284 (R. D.)	Mild exertional dyspnea for 18 months	31	M	None
4. 575-466 (F. L.)	Tumor detected in TB survey July, 1948; mild dysarthria and muscle weakness present at that time	58	M	Severe—minimal in morning but incapacitating in afternoon
5. 612-879 (C. J.)	Known myasthenia for 14 years; weight loss, 100 pounds in last 3 years	45	M	Chronic progressive resistance to drugs
6. 661-414 (J. A. N.)	Muscle weakness of 2 months' duration; no previous history	60	M	Acute onset at age 60 years
7. 678-562 (N. G.)	No symptoms; routine x-ray	43	M	None
8. 684-838 (R. P.)	Rejected by Army (age 17) after induction film revealed mediastinal tumor	23	M	None
9. 506-699	Seven months' history of progressive muscle weakness	58	M	Severe
10. 689-313 (O. R.)	Routine x-ray revealed mediastinal tumor; not present on film 1 year before	36	M	None

P.O. = postoperative

THYMIC NEOPLASMS

PATHOLOGIC FEATURES	METHOD OF DIAGNOSIS	TREATMENT	OUTCOME
Pleural implants right lympho-epithelioma type; late metastases in both pleural spaces	1. Right thoracotomy, Aug. 31, 1951 2. Transsternal thoracotomy, April 1, 1954	1. X-ray therapy Sept., 1951, with nitrogen mustard, 24 mg. 2. Surgical excision April, 1954	Good response to x-ray—HN_2 therapy Sept., 1951; myasthenia appeared with late metastases Feb., 1954; died in myasthenic crisis 3 days P.O.
1. Encapsulated anterior mediastinal tumor with calcific shell, apparently benign 2. Massive pericardial effusion with implants in pericardial sac; microscopic—thymic carcinoma	1. Excision tumor, July 20, 1949 2. Anterior thoracotomy plus pericardotomy, left, Nov. 28, 1952	1. Right thoracotomy with excision mediastinal tumor 2. Left anterior thoracotomy and pericardotomy; biopsy excision of intrapericardial implants	1. Uneventful convalescence and return to work 2. Prompt relief after pericardotomy; x-ray therapy (3,000 r) completed Dec., 1952; Patient is apparently well 2½ years after x-ray
Encapsulated, lobular mass; no evidence of metastases	Excision	Left thoracotomy and excision Dec., 1948; no P.O. therapy	Well 6½ years after excision
Encapsulated lobular mass; no invasion or metastases at surgery	1. Prostigmin test—dramatic response 2. Excision	Excision May, 1949, by sternal splitting approach, no P.O. radiation therapy	Prompt initial improvement, myasthenia returned in 6 months; late metastases (by x-ray) appeared May, 1952; died in myasthenic crisis, July, 1952
Gross extension by invasion and implantation of mediastinal tumor	Thoracotomy biopsy	Limited anterior thoracotomy for biopsy only Aug. 25, 1950	Hospital therapy with nitrogen mustard; died about 1 year later
Gross extension by invasion and implantation in mediastinum and right lung	Midline sternotomy biopsy	Sternotomy, April 8, 1952, inoperable, biopsy only; P.O. x-ray (2,500 r)	Good initial response with reduction in Prostigmin requirements; died suddenly March, 1953
Encapsulated, cystic degeneration	Excision	Left anterior thoracotomy and excision; no P.O. x-ray Oct. 23, 1952	Apparently well 2½ years P.O.
Lobulated mass with capsule invasion and invasion of pericardial fat and pleura; no implants seen	Excision, Feb., 3, 1953	Anterior thoracotomy Feb. 3, 1953, with excision of tumor and involved fat and pleura; P.O. x-ray (3,000 r)	Apparently well 2½ years P.O.
Encapsulated mass with central necrosis not obviously malignant	Autopsy, Dec., 1952		Died on medical service following curare test—apparently overwhelming aspiration of gastric contents
Encapsulated tumor mass with gross invasion of capsule and pericardial fat	Excision, March, 1953	Anterior thoracotomy March, 1953, excision of tumor; P.O. x-ray therapy begun (1,400 r)	Transferred elsewhere against advice—died May, 1953, with acute radiation pneumonitis

TABLE I

CLINIC NUMBER	CLINICAL HISTORY	AGE	SEX	MYASTHENIA GRAVIS
11. 689-132 (M. C.)	Developed progressive muscle weakness, Oct., 1952.	32	F	Moderately severe, not progressive
12. 626-941 (P. M.)	Tumor found Sept., 1949, treated for Hodgkin's disease (x-ray dose not known)	28	M	None
13. 696-317 (W. L.)	Tumor discovered on survey film	57	M	None
14. 702-058 (H. H.)	Unexplained fever, cough, weight loss—began 8 months before admission Cleveland Clinic Hospital	57	M	None
15. 651-982 (M. K.)	Unexpected x-ray finding during post-partum period, no associated symptoms	34	F	None
16. 717-542 (K. V.)	Unexpected x-ray finding. Patient admitted for cardiac study—mild exertional dyspnea and palpitation	25	M	None
17. 719-565 (E. B.)	Progressive swelling of head, neck and shoulders 3 months before admission (March 22, 1954) venous pressure 450 mm. H_2O	33	M	None
18. 740-934 (L. L.)	Progressive swelling of anterior chest wall over sternum with pleural effusion	65	M	None
19. 745-770 (C. B.)	Progressive swelling of head and neck; venous pressure on admission (March 29, 1955) 325 mm. H_2O. Normal x-ray April, 1954	31	F	None

—CONT'D

PATHOLOGIC FEATURES	METHOD OF DIAGNOSIS	TREATMENT	OUTCOME
Encapsulated tumor gross invasion of capsule and pericardial fat	Excision, April, 1953	Anterior thoracotomy April 6, 1953, excision of tumor; P.O. x-ray (4,500 r)	No change in myasthenia or Prostigmin requirements—required surgical drainage of pericardium May, 1954 (radiation effect)
Invasive tumor extending into right lung, pericardium, chest wall	Thoracotomy, Feb., 1951	Anterior thoracotomy Feb. 1, 1951; HN_2 therapy, followed 2 months later by x-ray therapy (2,200 r)	Progressive deterioration; contact lost and presumed dead
Lobulated tumor with gross capsular invasion	Excision, June 12, 1953	Anterior thoracotomy June 12, 1953; P.O. x-ray therapy (3,000 r)	Apparently well 2 years P.O.
Lobulated mass with invasion right hilum, pericardium, and chest wall	Thoracotomy, Aug. 26, 1953	Right thoracotomy Aug. 26, 1953; P.O. x-ray therapy (2,850 r); cobalt teletherapy given Jan. 10, 1955	Definite physical deterioration with evidence of local recurrence 1½ years after x-ray therapy—prompt regression with cobalt therapy
Lobulated mass with invasion of sternum, pleura, and pericardium	Thoracotomy, Nov. 19, 1951	Right thoracotomy Nov. 19, 1951; P.O. x-ray therapy (2,500 r)	Apparently well 3½ years P.O.; no further therapy given
Lobulated mass with invasion of pericardium and mid-mediastinum	1. Thoracotomy, Mar. 1, 1954 2. Submaxillary gland biopsy June 29, 1954	Right thoracotomy March 1, 1954; P.O. x-ray (3,000 r)	Initial response to x-ray was good; gland biopsy in submaxillary area (June 29, 1954) demonstrated cervical metastasis; rapid deterioration; died Aug. 23, 1954
Extensive malignant tumor of anterior mediastinum with superior caval obstruction	Trans-sternal biopsy Mar. 24, 1954	No thoracotomy; treated with x-ray therapy (3,050 r) completed April, 1954	Progressive improvement although venous pressure remains 350 mm. H_2O; x-ray shows regression of tumor after 18 months
Extensive neoplasm of anterior mediastinum with invasion of soft tissues, chest wall, and right pleural space	Needle biopsy chest wall Jan. 17, 1954	No thoracotomy; treated with cobalt teletherapy	Excellent initial response with regression of tumor and relief of effusion 2 months after therapy
Anterior mediastinal tumor with caval compression	Transsternal biopsy March 29, 1955	No thoracotomy; treated with cobalt teletherapy	Under therapy

In the 19 cases of thymic tumor which are presented, 16 proved to be malignant. The diagnosis of thymic neoplasm was established in every case by excision of the tumor or adequate tissue biopsy. The factor of malignancy was determined on the basis of the gross characteristics and the histopathologic features of the neoplasm. The criteria of malignancy in this series may be stated simply: (1) direct extension through the capsule into adjacent tissue, (2 intrathoracic implantation, (3) recurrence, and (4) distant metastases.

TABLE II. MALIGNANT FEATURES IN 16 THYMIC TUMORS

CRITERIA	NO. OF CASES
1. Direct extension	10
2. Pleural implantation	4
3. Recurrence	1
4. Distant metastases	1
TOTAL	16

By way of explanation, the listing in Table II is based on the single outstanding feature in each case (actually the majority presented more than one). The patient with implantation of a pleural space and secondary effusion has by necessity direct extension of the neoplasm through the capsule and adjacent pleura. Our tabulation does not describe the curious factor of localization presented by malignant thymic tumors. Only one patient demonstrated a distant metastasis (Case 16, K. Y.); a submaxillary lymphatic metastasis appeared several months prior to death. It is also of interest that 2 patients (Case 2, G. H.), and Case 4, F. L.) were operated upon for small encapsulated tumors that were considered benign in every respect. After apparently successful surgery, both patients demonstrated extensive implantation 3 years after operation (neither had received radiation therapy after surgery) (Fig. 1).

In this series, the resected neoplasms were for the most part not large, 12 cm. being the greatest diameter encountered. Grossly, the tumors often appeared to be encapsulated by the contiguous mediastinal tissues and anterior pleura removed with them. The cut surfaces were not in any way distinctive for any cell type and a wide variety of configurations were seen. Two of the neoplasms were cystic; one (Case 2, G. H.) so completely so that only small cell nests could be seen beneath a partially calcified capsule, and at that time, a definite histopathologic classification was not possible. This patient returned 3 years later with local and intrapericardial metastases. The solid tumors had varied homogeneous, granular, or bosselated surfaces. They were relatively firm and ranged in color from white through various shades of yellow and tan to a salmon pink.

In addition to those features previously mentioned, the neoplasms possessed certain histologic features in common. Many of the tumors demonstrated a marked tendency to incorporate within their confines the surrounding fatty tissue and to show evidence of subendothelial bulging of the wall in small veins of the immediately adjacent tissue (Fig. 2). The significance of this latter is not completely understood unless it bears the same connotation as is found in such neoplasms as the encapsulated angio-invasive carcinoma of the thyroid.

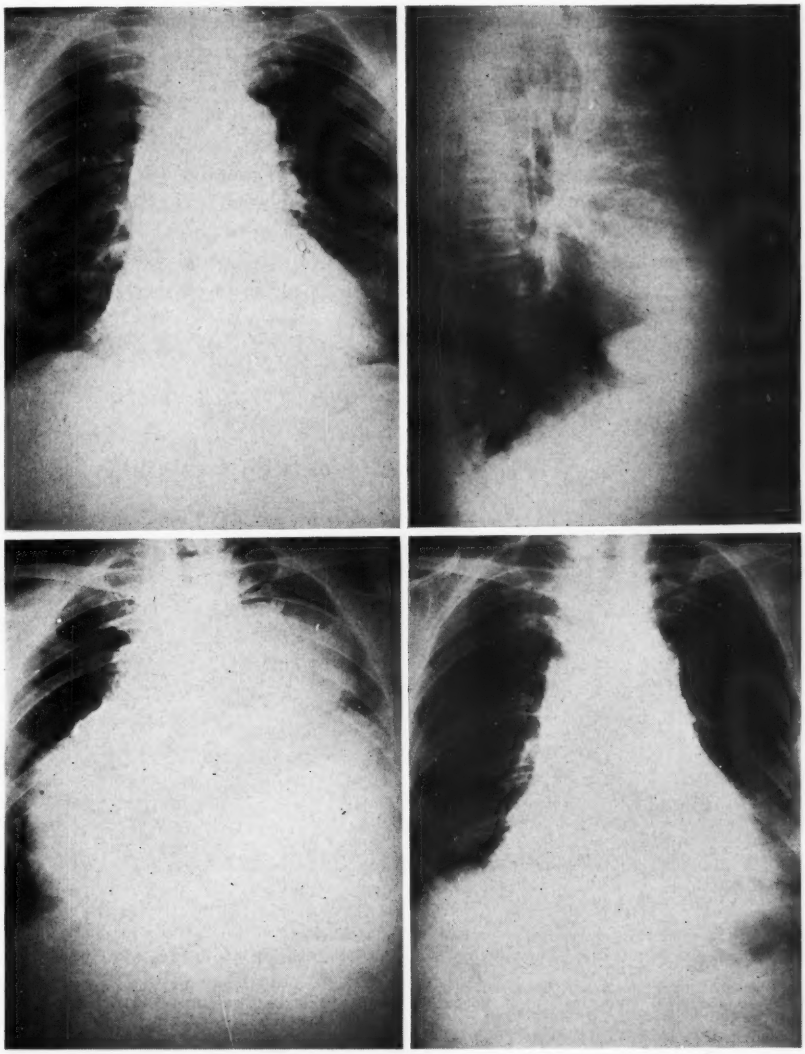
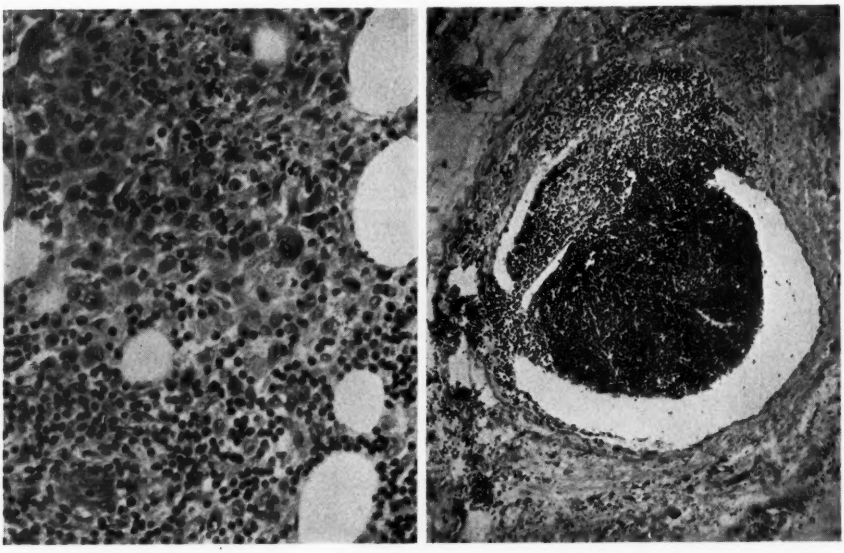


Fig. 1.—(Case 2; G.H.) The roentgenograms at top demonstrate the thymic neoplasm of the anterior mediastinum as it appeared in July, 1949.

Lower left is the reproduction of film made in November, 1952. The tremendous cardiac silhouette is produced by a massive effusion secondary to interpericardial implants. Evacuation of the effusion and biopsy of the interpericardial implants were performed by surgical pericardotomy.

Lower right is reproduction of film taken March, 1955, two and one-half years after radiotherapy. The patient remains clinically well.

It obviously must represent some mechanism of farther growth and spread of the neoplasm; however, gross intravascular extension is not a feature of these tumors. Apart from the cystic neoplasms encountered and the Hodgkins subgroup to be discussed, necrosis was not a feature of these tumors. The stromal arrangements were quite similar in most respects; broad bands of collagen tended to subdivide the neoplasms into smaller lobules. For the most part, this connective tissue was rather dense; but in 2 cases, focal areas showed what we have designated as stromal hyperplasia. Small spindle cells were greatly increased in number in the interstices of the 2 neoplasms and at times appeared to invade the adjacent tumor tissue proper and to form small whorls. Lowenhaupt[2] has considered these cells to be a form of epithelial proliferation, but we are more inclined to look upon them as abnormalities of the stroma. With



A. *B.*

Fig. 2.—Microscopic evidence of aggressive nature of the tumors.

A, (Case 10; O.R.) Photomicrograph showing invasion of fatty tissue by Hodgkin's variety. (Hematoxylin and eosin ×285; reduced ⅙.)

B, (Case 13; W.L.) Photomicrograph demonstrating subendothelial bulging by lymphocytes in marginal condensation of fibrous tissue (capsule) of neoplasm. (Hematoxylin and eosin ×80; reduced ⅙.)

phosphotungstic acid—hematoxylin stains, the individual cells possessed fine fibrils, compatible with those of fibroblasts, and in the maturing areas, deposition of collagen was a constant feature as demonstrated by the Masson's polychrome stain. This stromal hyperplasia can be very confusing. We recently encountered a case in which stromal hyperplasia was so marked that fibrosarcomatous change was suggested. The lesions in general showed a great deal of mitotic activity scattered throughout the parenchyma.

TABLE III. NEOPLASMS OF THYMIC ORIGIN

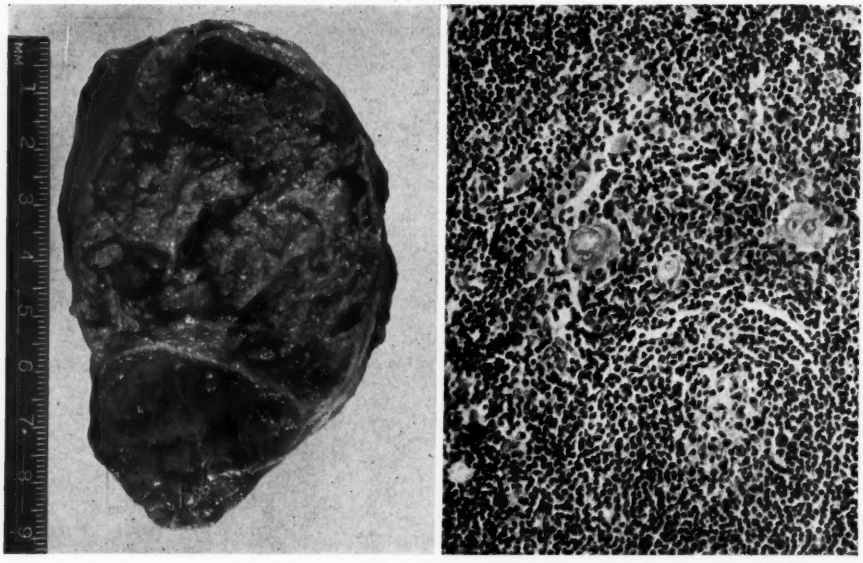
	NO. OF CASES	TOTAL
1. Lymphomatous type		
a. Lymphocytic variant	6	
b. Hodgkin's variant	3	
		9
2. Carcinomatous type		
a. Lympho-epithelioma	6	
b. Epithelial variant	4	
		10

A classification of the histopathologic features encountered in the study of thymic neoplasms has intrigued pathologists for many years. The study of Margolis[4] offers an example of the difficulties encountered earlier in classification. Lowenhaupt[2] has been the most recent of the writers to present an involved table of nomenclature. Seybold and co-workers,[6] Ackerman,[9] and we find her classification interesting, but of relatively little value so far as the neoplasms are concerned. We do believe, however, that one may be more definite in classification and not be limited to the observation that neoplasms are either predominantly lymphocytic or predominantly epithelial. We agree with the general statements that neoplasms are very difficult to categorize, as they show a reluctance to present themselves as pure forms which can be easily compartmented. The problem of being able to distinguish between the benign and malignant thymoma on a histopathologic basis is very real; all have the ability to be aggressive regardless of the classification groups. Consequently, we have considered them all as of malignant potential and believe that *malignant thymoma* should be the term utilized for general classification.

We have divided the malignant thymomas into 2 subgroups: (1) the lymphomatous type, and (2) the carcinomatous type. In so doing, we have been content to accept the theories that the thymus is an endodermal derivative basically possessing a supporting framework of epithelial cells which may become rather reticular in appearance. The lymphocytic component represents secondary infiltration of the organ and the small round cells are truly lymphocytes.

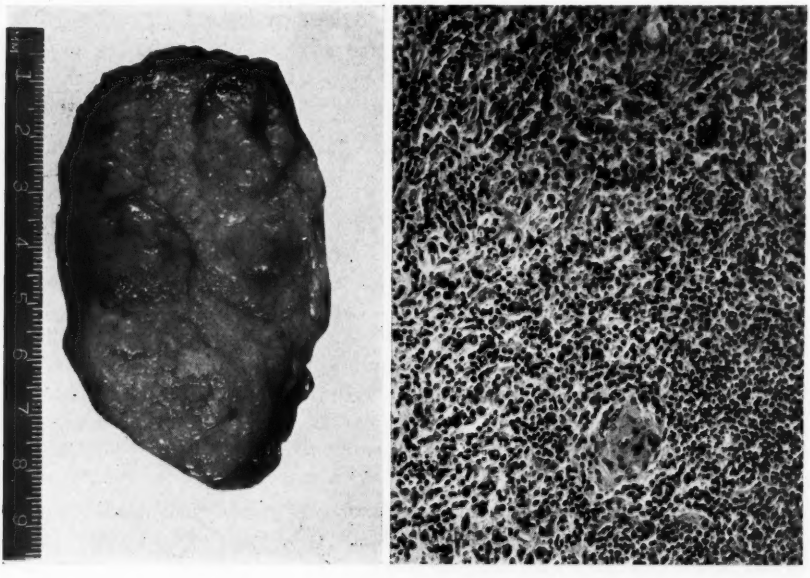
1. *Lymphomatous Type.*—Nine of the cases have been classified in the lymphomatous subdivision, that was further subdivided into the lymphocytic and the Hodgkin's type. In 6 of the cases, the cellular component encountered was almost completely lymphocytic (Fig. 3. We do not say that these neoplasms were completely lymphocytic, as one may encounter in the background an occasional reticular cell; small proliferative cell nests, resembling epithelial cells, to be described later, occur along the blood vessels. We have not been disturbed by their presence as they represent a rare component but are comforted by them as they constantly indicate that the thymus was the source of the neoplasm.

The second subdivision of the lymphomatous group encompasses 3 cases catalogued as malignant thymoma, Hodgkin's type (Fig. 4). In our earlier experience, we can recall certain neoplasms, fatal in their outcome, that were apparently limited to the anterior mediastinal structures which we considered as a localized form of Hodgkin's disease. It is likely that these cases were



A. *B.*

Fig. 3.—(Case 7; N.G.) Lymphocytic variant. *A*, Gross tumor is predominantly cystic with necrotic wall. The viable homogeneous portion is at inferior pole. *B*, Photomicrograph showing tumor composed predominantly of small lymphocytes. Rare abortive Hassall's corpuscles included to show their presence. (Hematoxylin and eosin ×210; reduced ⅙.)

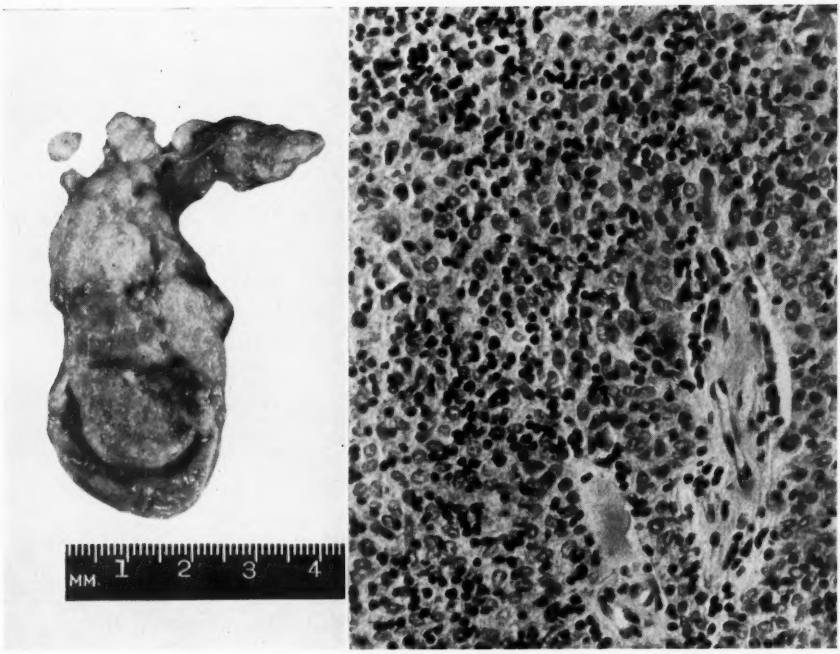


A. *B.*

Fig. 4.—(Case 10; O.R.) Hodgkin's variety. *A*, Gross specimen demonstrating lobulated cut surface. *B*, Photomicrograph demonstrating pleomorphic cytology including multinucleate Sternberg-Reed cells. Note bizarre Hassall's corpuscle in lower portion of field. (Hematoxylin and eosin ×160; reduced ⅙.)

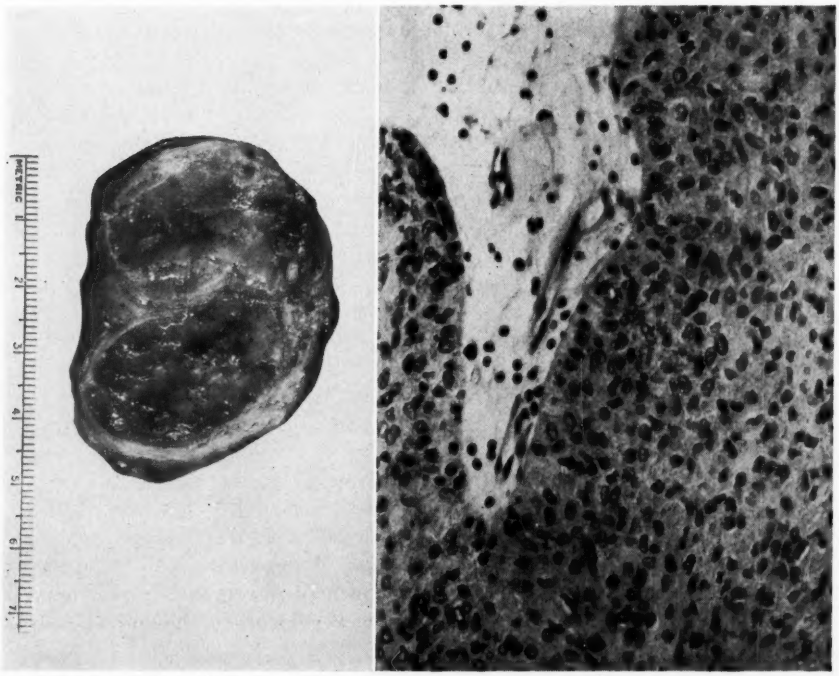
examples of the disorder limited to the thymus. All of the present 3 cases show histologic features in common. Characteristically, the tumors are made up of conglomerate foci that appear to be passing through certain histologic changes. The earliest features seemed to be the formation of cellular aggregates surrounded by small lymphocytes. These cellular aggregates superficially resembled germinal centers, but are characterized by a markedly polymorphous cytology. Cells with sparse cytoplasm and irregularly oval or lobulated nuclei, and at times prominent nucleoli, are common. In addition, multinucleated giant cells with more abundant gray cytoplasm and vesicular nuclei, indistinguishable from Sternberg-Reed cells, were found. They show an absence of any staining properties of their cytoplasm by the periodic acid-Schiff method. Later, central necrosis apparently occurs within the cellular aggregates, and macrophages with more abundant pink-staining cytoplasm and round or oval vesicular nuclei appear. Still later, deposition of collagen is present in the necrotic areas. The necrotic stage superficially resembles granulomatous change and hence the term "granulomatous thymoma," a rather poor designation for the neoplastic disorder. These neoplasms, however, still possess the propensity to form bizarre Hassall's corpuscles. The source of this particular subgroup is again a philosophic question at the present time. Whether they are a peculiar transformation of the supporting cells of the thymus or truly lymphomatous neoplasm is a point of debate. We have favored the latter by designating it as a Hodgkin's variety.

2. *Carcinomatous Type.*—The second major subdivision of malignant thymomas, the carcinomatous variety, is characterized by prominence of the thymic epithelial cell. There appear to be 2 subvariants of the carcinomatous type: (1) lympho-epithelioma, and (2) the epithelial variant. The lympho-epithelial group contains 6 cases, all of which were characterized by a definite admixture of true cytologic forms (Fig. 5). The small, round, densely staining lymphocyte was ever present in varying amounts and intermingled with cells possessing round, oval, or slightly lobulated vesicular nuclei, and only a sparse amount of cytoplasm. This epithelial cell, although present in large numbers, may at times be rather small and not quickly recognized, but at other times is rather large in proportion to the lymphocyte. They are dispersed in small nests, larger sheets, and at times are quite prominent along small vessels. The epithelial carcinomatous variety is merely one step further along the scale. Four cases have been catalogued as belonging to this group. The neoplasms are characterized by the presence of large syncytial masses of cells forming the entire neoplasm (Fig. 6). A moderate amount of pink-staining cytoplasm is present, but cell boundaries are very indistinct. The nuclei are round or oval, and pale staining for the most part. The continuous masses are usually sharply demarcated from the small vessels and there is a tendency for the nuclei to palisade around the vessels. We have been unable to substantiate any evidence of cyst formation within this group of neoplasms. Lymphocytes still are present, but are very sparse in number and merely scattered discriminately throughout the tumor. Occasionally these tumors do show evidence of having Hassall's corpuscle formation.



A. *B.*

Fig. 5.—(Case 1; G.L.H.) Lympho-epithelial variant. *A*, Gross specimen is partially necrotic and cystic; radiation therapy applied two and one-half years prior to removal. *B*, Photomicrograph of mixture of small, dark-staining lymphocytes and larger indistinct cells with pale round or oval large nuclei. (Hematoxylin and eosin ×285.)



A. *B.*

Fig. 6.—(Case 11; M.C.) Epithelial variant. *A*, Small apparently encapsulated neoplasm with faintly lobulated surface. *B*, Syncytial is sharply marginated from vascular stroma. A suggestion of peripheral palisading is present; note absence of cellular outlines. (Hematoxylin and eosin ×285.)

We recognize that this classification may be an arbitrary one and that all of these neoplasms may represent segregated stages of the same process. However, it does lend order to our clinical and histopathologic findings. As a classification, it offers little of prognostic significance. It is our hope that it may contribute to the most important phase of the problem, recognition that a tumor is of thymic origin and with malignant potentiality.

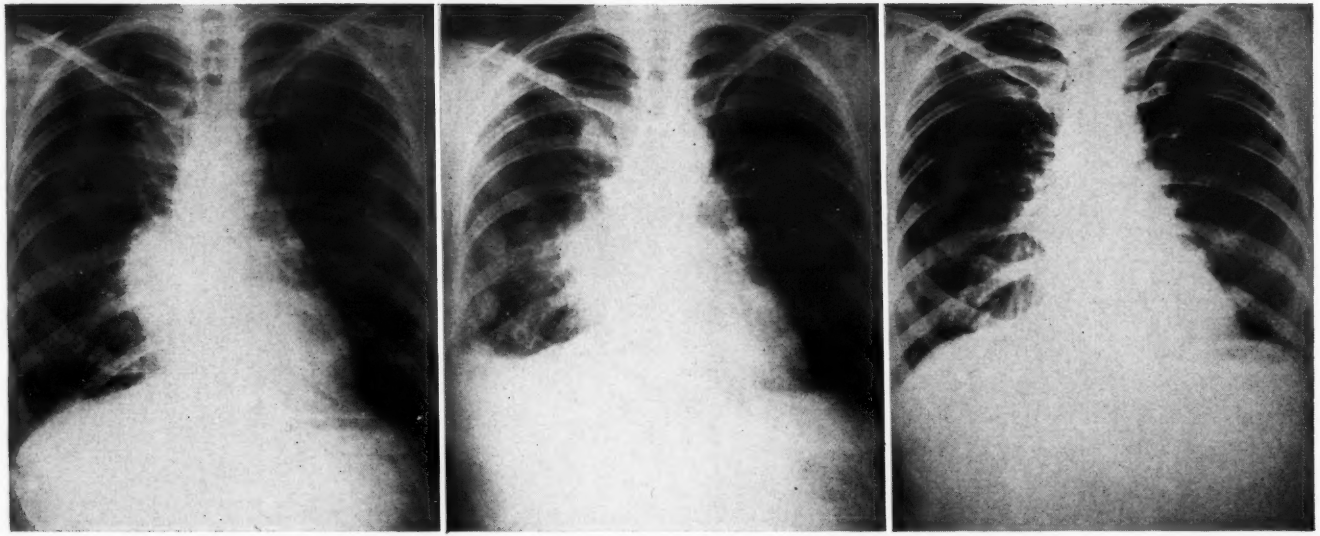
TREATMENT

The presence of myasthenia gravis is not the primary indication for therapy; it does impose an added hazard and, in some instances, an insurmountable barrier to tumor eradication. Treatment of a thymic neoplasm as a phase in the therapy or the prevention of myasthenia gravis is of secondary import. The essence of therapy in thymic neoplasm, as in all mediastinal tumors, should be directed toward cancer control.

There are 3 basic approaches in the management of thymic neoplasms: (1) biopsy, (2) surgical excision, and (3) radiation therapy. In each case 1 or all 3 approaches to therapy are indicated.

Biopsy.—Diagnosis of a primary thymic neoplasm is dependent on histopathologic examination. The ideal method of obtaining tissue is by extracapsular "enucleation" of the entire mass. When there is radiographic evidence of implantation, or there is evidence of malignant extension by superior caval obstruction or penetrating chest wall invasion, a less inclusive form of biopsy is indicated. Such biopsy requires a direct approach by one of three methods: (1) thoracotomy or suprasternal incision, (2) needle biopsy, or (3) transsternal biopsy. We have used a limited anterior thoracotomy approach under local anesthesia in 3 patients where the evidence suggested neoplasm immediately below the chest wall and lateral to the sternal border. Needle biopsy has been employed once (Case 18, L. L.), the tumor had penetrated the anterior chest wall and could be felt in the soft tissues overlying the sternum. In 2 cases of superior caval obstruction (Case 17, E. B., and Case 19, C. B.), we have employed transsternal biopsy. This is a relatively simple and highly effective method of obtaining tissue without resorting to thoracotomy (Fig. 8). It appears unlikely that less direct methods such as scalene node biopsy will be effective in thymic tumors as lymph node extension is not common.

Surgical Excision.—Ideal therapy of a neoplasm requires total removal accomplished without violation of tumor boundary and leaving no residual cell remnants. Nine of the 19 patients in this series had surgical extirpation of their tumors; 1 died in an acute postoperative myasthenic crisis, 6 are living and apparently free of neoplasm; 2 had late recurrences of neoplasm after removal of apparently benign tumors. From the technical standpoint, excision of a thymic neoplasm is usually not difficult even when there is extracapsular invasion of the fat and pericardium. In 2 of the early cases, we employed midline sternotomy which is unnecessary and only adds to the morbidity and the complexity of the operation. For most thymic tumors, adequate exposure is obtained through either a right or left anterior thoracotomy approach. If it should be necessary, the incision can be extended by transection of the sternum.



A. *B.* *C.*

Fig. 7.—(Case 1; G. L. H.) Pictorial sequence of highly malignant thymic neoplasm with pleural implantation and favorable response to radiation therapy. *A*, A reproduction of film made in February, 1951. There were no symptoms of the large anterior mediastinal tumor; a previous film, date 1947, was entirely normal. *B*, Film demonstrates multiple intrapleural metastases that appeared in August, 1951. The radiographic appearance of these implants was preceded by abrupt onset of pain corresponding to phrenic distribution on the right. Thoracotomy biopsy established diagnosis of metastatic thymic carcinoma. *C*, A film made in February, 1954, following combination of radiation therapy and nitrogen mustard therapy. Shortly after this film was made, the patient died in severe myasthenic crisis. (See Table I.)

Radiation Therapy.—There is reason to believe that some neoplasms of the thymus have a tendency to regress under radiation therapy and that local implants frequently share this property. There is no way of anticipating tumor response until a full course of therapy has been given; therefore, we urge that all patients who present a nonresectable neoplasm be given a full course of radiotherapy, rather than a test dose. Of the 19 patients in our series, 10 had

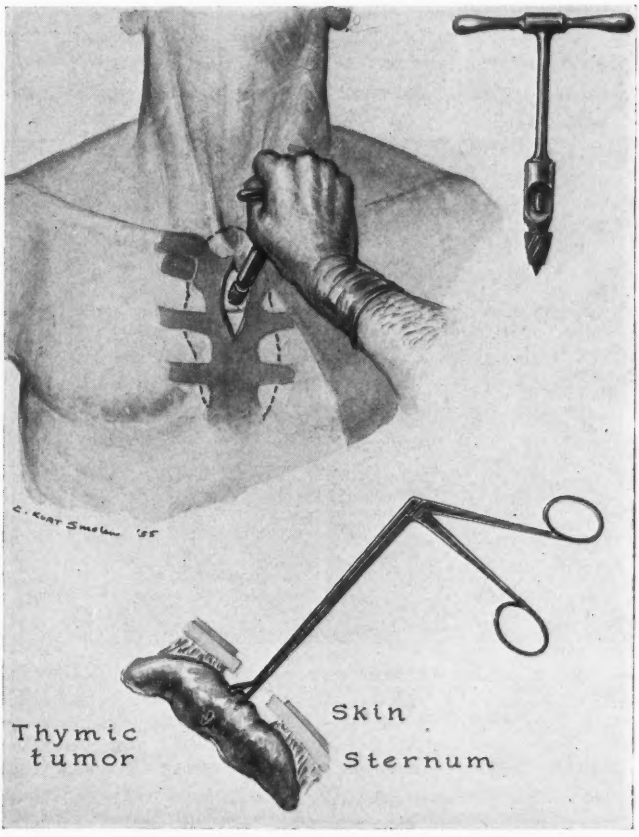


Fig. 8.—Diagrammatic description of technique employed in transsternal biopsy of thymic neoplasms. This method is usually employed only in large anterior mediastinal tumors which are clinically malignant and inoperable. In properly selected cases the technique is safe, as the neoplasm lies between the sternum and the great vessels of the mediastinum. The procedure is performed under local anesthesia.

nonresectable neoplasms. All of these received radiation therapy with completely unpredictable results. One patient (Case 15, M. K.) is in excellent health three and one-half years after receiving 2,500 r of therapy for a highly malignant nonresectable lesion. There is little question that the majority have received benefit and prolongation of life (see Table II).

After reviewing our limited experience, since 1949, with the 19 cases presented, we believe that ideal therapy consists of surgical extirpation of the primary neoplasm followed by a full course of radiation therapy to the anterior mediastinum. It is obvious that we cannot distinguish the benign from the malignant tumor by histopathologic study. It is apparent likewise, that gross diagnosis of a benign thymic tumor is unreliable. Two of the "benign" thymomas presented metastases, two and one-half and three years after excision. We have adopted the philosophy that all thymic tumors are malignant or of malignant potentiality and consider the ideal treatment to combine excision with a full course of radiation therapy to the anterior mediastinum. The radiotherapy should begin during the immediate postoperative phase. It might well

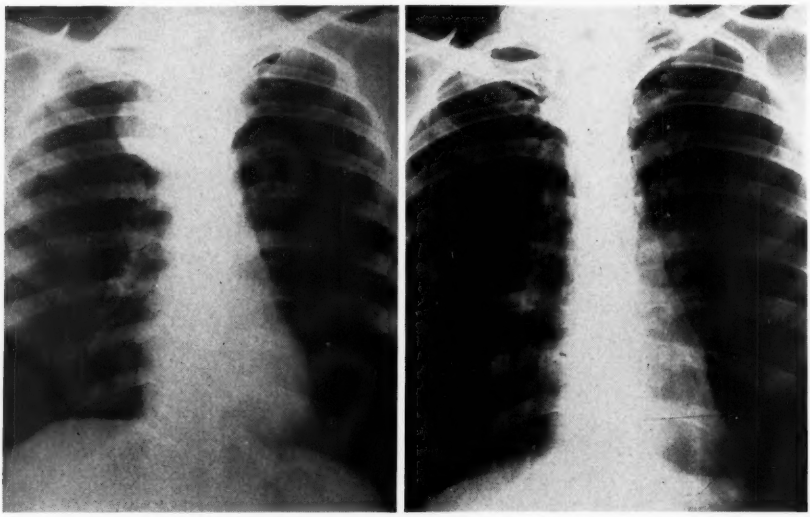


Fig. 9.—(Case 15; M.K.) *A*, Roentgenogram demonstrates malignant thymoma that was accidentally discovered during immediate postpartum. Tissue diagnosis established by limited anterior thoracotomy. *B*, Radiographic appearance of chest approximately four and one-half years after radiation therapy. The patient remains clinically well.

be argued that successful extirpation of the tumor would permit the surgeon to allow a period of clinical observation before employing radiation therapy. It is our contention, however, that the period of time which may elapse before late metastases appear may well go beyond the period of clinical observation and contact between surgeon and patient may be broken. This, in addition to bitter experience with 2 late recurrences in patients presumed to be cured, makes us believe that radiation therapy in the immediate postoperative phase is an integral part of therapy for all thymic neoplasms.

SUMMARY AND CONCLUSIONS

Twenty-six case histories were reviewed: 19 are believed to be thymic in origin and 7 to be intrathymic in locale, but not of truly thymic origin. The

factor of malignancy predominates in this personal series, although it was not immediately apparent in every case. It is our conviction that thymic tumors are malignant or potentially malignant, and that the cancer factor is of greater importance than any possible relationship with myasthenia gravis.

Response to therapy is unpredictable regardless of whether the tumor is apparently benign or obviously malignant. A tissue specimen is mandatory for diagnosis and may be obtained by several biopsy methods including the simple expedient of transsternal biopsy. We believe that every patient who has a nonresectable thymoma should be given a full course of radiation therapy. All patients who have undergone thymectomy should receive radiation therapy to the mediastinum to reduce the hazard of late recurrence.

We believe that thymic neoplasms may be classified as of 2 types: the lymphomatous, and the carcinomatous. Employment of this classification and its variants has no value in prognosis but may improve diagnosis of primary thymic neoplasm.

REFERENCES

1. Blalock, A.: Thymectomy in Treatment of Myasthenia Gravis: Report of 20 Cases, J. Thoracic Surg. **13**: 316-339, 1944.
2. Lowenhaupt, E.: Tumors of Thymus in Relation to Thymic Epithelial Anlage, Cancer **1**: 547-563, 1948.
3. Murray, N. A., and McDonald, J. R.: Tumors of the Thymus in Myasthenia Gravis, Am. J. Clin. Path. **15**: 87-94, 1945.
4. Margolis, H. M.: Tumors of Thymus: Pathology, Classification and Report of Cases, Am. J. Cancer (supp.) **15**: 2106-2142, 1931.
5. Miller, S. E., and Redisch, W.: Malignant Thymoma in Case of Myasthenia Gravis, Ann. Int. Med. **26**: 440-448, 1947.
6. Seybold, W. D., McDonald, J. R., Clagett, O. T., and Good, C. A.: Tumors of the Thymus, J. Thoracic Surg. **20**: 195-213, 1950.
7. Binkley, F. M., Thornburn, J. D., Stephens, H. B., and Grimes, O. F.: Mediastinal Tumors of Thymic Origin, California Med. **78**: 267-273, 1953.
8. Poer, D. H.: Effect of Removal of Malignant Thymic Tumor in Case of Myasthenia Gravis, Ann. Surg. **115**: 586-595, 1952.
9. Ackerman, L. V.: Surgical Pathology, St. Louis, 1953, The C. V. Mosby Co., p. 197.

Discussion

DR. JOHN W. STRIEDER, Brookline, Mass.—I should like to compliment the essayists on the handling of a difficult and obscure subject, and particularly on their classification. I wish to call attention to two aspects, one of which is well known and the other, perhaps, not so well known. Dr. Effler mentioned that patients with thymic malignancies may later develop myasthenia gravis. We have had one such patient from whom a thymoma was removed and who two years later developed myasthenia gravis. A year later, after considerable therapy, she had a total thymectomy with complete remission for two years up to this time.

The occurrence of a so-called benign thymoma and of a refractory anemia which failed to respond to all therapeutic measures has been observed in 2 patients at the Massachusetts Memorial Hospitals. The simultaneous occurrence of two unusual pathologic states in 2 patients in a relatively brief period suggests a probable relationship between the thymic tumor and erythropoietic abnormality, a probability which was strengthened by finding several cases in the literature. This unusual coincidence of abnormalities in the thymus and in the blood provides one more link in the legendary and frequently nebulous chain of evidence connecting the thymus gland with the hematopoietic system. Both these patients were women aged 40 and 45, respectively, and both ultimately had excision of the thymoma without apparent effect on the course of the anemia. Both have continued to run a course which has been characterized by failure to form blood. At least 150 to 200 transfusions, mostly of

packed red cells, have been given in each case. The patients are both developing evidence of hemochromatosis on the basis of transfusions. It would appear, from considerable investigation, that the simultaneous chance occurrence of these two entities, that is, thymoma and anemia, would be extremely rare. The thymus gland was not removed at the time the thymic tumors were resected, and the possibility must be considered that the persistence of thymic tissue may have a continuing adverse influence on erythropoiesis. It is interesting to speculate as to the possible beneficial effect that removal of the thymus gland itself might exert on our patients and in certain other cases of refractory anemia. I hope I can report on that later. In view of the marked clinical improvement which has been known to follow resection of thymomas in 3 similar cases, the advisability of surgical exploration and possible resection of the thymus should be considered in patients with refractory anemia, particularly in those with hypoplasia or aplasia of the erythropoietic element of the bone marrow.

DR. JOHN G. CHESNEY, Miami, Fla.—I wish to show slides of a case which I think is quite unique. This is a 21-year-old girl with no complaints, whose lesion was found on routine chest survey. This rounded lesion was found on the right side. She was operated upon and the lesion was found to be deep in the major fissure under the pleural reflection in the fissure. It lay in the anterior segment of the upper lobe and was directly related to the posterior portion of the middle lobe, and also related directly to the anterior portion of the superior segment of the lower lobe. The lesion was dissected from its bed without difficulty. It was necessary to strip off the adventitia of the lower lobe artery and what our pathologist has described as normal-appearing thymic tissue was found.

(slide) Here is a high-power section of the same tumor, which I think is unique. At least, I know of no reported ectopic thymic tissue in the lung.

DR. JAMES E. DAILEY, Houston, Tex.—I would like to report an experience with a total of 12 thymoma cases, 9 of which were benign and 3 malignant. Only 2 of this group had myasthenia gravis.

(slide) This was a 57-year-old Negro who falls into the classification Dr. Effler described, a carcinomatous type. Incidentally, this patient was operated upon in 1949 and is still alive.

(slide) The next one, a 45-year-old white man also had a carcinoma of the thymus. He died shortly after operation with a sudden massive pulmonary embolus.

(slide) This 41-year-old white woman had what the pathologist described as being in the borderline group between the noncancerous and the malignant thymoma of the type of Symmer. She died within a year from metastatic lymphosarcoma.

(slide) This next is a most interesting case. In this you will note the thin density of the tumor; it was a lipoma. The dark areas can be identified microscopically as typical thymus tissue. The diagnosis was benign lipoma of the thymus gland.

I am not sure that I would go along with Dr. Effler on x-ray therapy for *all* thymomas.

DR. HARVEY J. MENDELSOHN, Cleveland, Ohio.—I wish to compliment Dr. Effler on his excellent presentation and classification of this confusing subject of thymic tumors. There is one complication which he had occasion to encounter only once in our series of 13 cases of thymic tumors, 8 of which were malignant. This occurred in a child, aged 5 years, with a lymphosarcoma of the thymus. There was a history of six days of upper respiratory obstruction; he had been in good health otherwise until then. The problem, of course, was to treat the respiratory obstruction and to treat the tumor. Surgical incision was contraindicated and it was chosen to give him x-ray therapy. He died suddenly in thirty-six hours of respiratory obstruction after one x-ray treatment of 100 r, and before tracheotomy could be established.

Autopsy showed a lymphosarcoma surrounding the trachea and great vessels and filling the region normally occupied by the thymus.

Within a few weeks another child was admitted to the hospital with anatomically the same situation; however, he had leukemia. He had the same type of respiratory obstruction, and in this case we heeded the warning of Dr. Neuhauser of Boston and treated this child with cortisone. The tumor receded within forty-eight hours and the respiratory obstruction was relieved. I wish to mention the lympholytic effect of cortisone as an adjunct in treat-

ment of patients who have this problem. It does not always produce regression of thymic tumors or lymphomas but should be tried when respiratory obstruction is present. It should be followed quickly by x-ray or nitrogen mustard therapy since the cortisone effect is temporary.

DR. JOHN F. HIGGINSON, Portland, Ore.—We have 2 cases of thymic neoplasms to mention. One of these typifies the multiple mistaken diagnoses mentioned by the authors as frequent. This patient had a large anterior superior mediastinal mass and several other masses in the left lung field on chest x-ray. Bronchoscopy yielded a bronchial aspirate suspected of showing possible bronchiogenic carcinoma. Left pleural fluid contained only mesothelial cells. Thoracotomy demonstrated multiple tumors throughout the left chest and lung and a large mass in the anterior superior mediastinum. The tissue removed for biopsy was diagnosed on frozen section as metastatic bronchiogenic carcinoma. Later the fixed sections were felt to demonstrate a malignant thymoma. Still later the pathologist changed to a diagnosis of liposarcoma, but following review of the sections throughout the country the lesion was felt to be a malignant thymoma.

The second case is that of a lipoma of the thymus in a 13-year-old boy. This anterior mediastinal tumor weighed 589 Gm. and the pathologist was explicit in stating that the tumor was a lipoma of the thymus and not a simple mediastinal lipoma encroaching upon thymic tissue. No evidence of malignancy was found in this tumor.

DR. HOWARD K. GRAY, Rochester, Minn.: We would certainly agree with Dr. Effler and Dr. McCormack that tumors of the thymus occur more frequently than has generally been appreciated. Since 1940, approximately 75 patients with tumors arising from the thymus have been operated upon at the Mayo Clinic. We believe thymic tumors occur even more frequently than dermoid and teratoid tumors, which are usually considered to be the most common anterior mediastinal tumors.

While the relationship between myasthenia gravis and thymic tumors is poorly understood, it is very real and significant. It cannot be pure coincidence that thymic tumors have been found in 16 per cent of almost 500 cases of myasthenia gravis seen since 1940, or that approximately 70 per cent of all our thymic tumors have occurred in individuals with myasthenia gravis. Of considerable interest, too, is the fact that we know of 5 cases in which patients who had never had myasthenia gravis previous to removal of a thymic tumor have developed typical myasthenia gravis at various intervals after removal of the thymic tumors.

Whether thymic tumors should be considered as benign or malignant depends on one's definition of what constitutes benignancy and malignancy. Certainly they are a unique group of tumors. Microscopically they look as if they should be benign. Many show cystic changes and areas of calcification and are well encapsulated, and both grossly and microscopically appear to be entirely benign. However, in other cases a tumor that is identical on microscopic examination will invade through the pleura and into the lung, invade through the pericardium, obstruct the large veins in the mediastinum, and implant on pleural surfaces, producing a bloody pleural effusion. It has been an observation of interest to us that thus far we have not seen a true thymic tumor that has metastasized or spread outside the thorax.

It has been our practice to treat thymic tumors that have shown invasive characteristics with intensive deep x-ray therapy postoperatively. We have not used deep x-ray therapy postoperatively in patients with well-encapsulated tumors. We have not encountered late metastases or recurrence in these apparently well-localized tumors.

The effect of deep x-ray therapy on tumors of the thymus that could not be resected has been rather unpredictable in our experience. In some it has apparently been quite effective. In other cases that seemed to be identical, x-ray therapy has apparently not been of much value.

DR. JOHN L. POOL, New York, N. Y.: There are two points I should like to make on this extremely complete presentation of the subject of thymomas. In the first place,

the malignancy of these lesions has been seen in the experience at Memorial Center in very much the same way as presented here today, and we agree that postoperative radiation therapy is a useful adjunct in cancer of the thymus gland, which so often has a histologic appearance similar to the lymphomatous neoplasms. The solid tumor of the thymic gland lies in the anterior mediastinal fat and it can be noted to infiltrate the perithymic fat without any clearly defined capsule. In one instance, a man in his twenties had a cystic thymic carcinoma apparently totally extirpated. The lesion was asymptomatic and found by chance. The excision was followed by radiation therapy and seven years later metastasis to the axilla was noted without any mediastinal recurrence. Another aspect of the natural life span of these neoplasms is represented by a 39-year-old woman who had myasthenic symptoms in 1950, and a chest x-ray at that time revealed an anterior mediastinal tumor with a sharply defined border, apparently 6 cm. in diameter. She was treated with Prostigmin for four and one-half years at which time repeat chest x-rays revealed the margin to be "shaggy" and to have a definite projection at one point. At this time she came under our care and exploratory thoracotomy revealed reticulum-cell lymphosarcoma with infiltration of adjacent lung. Malignant degeneration had apparently occurred during the intervening years. These findings reinforce to me the advisability of early excision for all undiagnosed anterior mediastinal masses.

DR. DE WITT C. DAUGHTRY, Miami, Fla.—Of our 8 cases of thymoma, 4 have been classed as malignant by our pathologists. All, except 1 patient, are alive one to eight years following surgery. The death was in a terminal case when first seen and no surgery or other therapy was recommended. One other had such extensive invasion of the mediastinum that surgical removal could not be accomplished. This was complicated by superior vena caval obstruction. Despite the extensiveness of this lesion, the patient is alive and apparently well seven years after surgery and x-ray therapy. It has been necessary to give him two courses of x-ray therapy.

Four tumors were in the usual location for thymomas while the remaining four were located elsewhere; 1 in the lower anterior mediastinum, 1 in the posterior mediastinum, and 2 within the lung. My associate, Dr. Chesney, has already mentioned one of them in some detail. The other one was cystic and located in the mid-lung field. Two of our patients complained of excessive fatigability over a period of four or five years which necessitated change in their occupation. This symptom has completely subsided in both of them since surgery.

There is no question but that thymic tumors should be explored and removed immediately upon discovery if possible. In addition, it seems wise even if complete extirpation can be accomplished to use x-ray therapy if there is any question of malignancy.

DR. J. HARVEY JOHNSTON, JR., Jackson, Miss.—Admittedly, the results of thymectomy in myasthenia gravis are unpredictable. There is increasing evidence, however, that thymectomy often effects amelioration of symptoms and occasionally cure in myasthenia gravis.

I should like to record the case of a 35-year-old white woman admitted in extremis in an acute myasthenic crisis despite 4 mg. of Prostigmin every hour by injection. Emergency tracheotomy was done which aided in evacuation of viscid tracheobronchial secretions and more effective ventilation. Despite large doses of Prostigmin and meticulous attention to tracheobronchial secretions, her condition remained critical—so much so, that all observers felt that death was inevitable with continued conservative treatment. Thus, with considerable trepidation, emergency thymectomy was performed and a well-circumscribed 8.5 by 6.5 by 3 cm. thymoma was removed and a thymic remnant was removed. The procedure was technically easy and tolerated well by the patient. The response after surgery was indeed gratifying with rapid and progressive improvement allowing return to full activity one month later on a maintenance dose of 30 mg. of oral Prostigmin per twenty-four hours.

Although this excellent result may be only a fortuitous one, it suggests that early thymectomy with the aid of tracheotomy after a short period of intensive preoperative preparation may be lifesaving in severe cases of myasthenic crisis.

DR. EDGAR W. DAVIS, Washington, D. C.—We too have been quite disturbed by the confusion and uncertainty about thymic neoplasia. In the brief time available I would like particularly to stress the too little appreciated tendency toward cyst formation. Small cysts which are so typical of thymomas cause no diagnostic difficulty, but when the cystic element predominates, the thymic origin of the tumor may be completely missed. Actually these "thymic cysts" have received scant attention in the literature, so much so that perhaps the most famous such specimen, namely, the one removed by Dr. Blalock in his first thymectomy for myasthenia gravis, has been overlooked in all recent reviews on the subject. We seriously question whether such cysts are as rare as the literature suggests in view of 5 thymic cysts among our personal series of 17 thymoma cases.

(Slide) This is the chest x-ray of a 10-year-old boy. This mediastinal mass had been discovered in a fortuitous roentgenogram taken several years earlier, and because of the likelihood of its representing an enlarged thymus gland, he had received small amounts of x-ray therapy. Ultimately, however, its increasing size prompted its resection. Grossly, it was a thin-walled multilocular cyst containing clear fluid. The significance of the thymic tissue throughout the septa was appreciated only recently when the sections were re-examined.

(Slide) This 24-year-old medical student presented a comparable negative history and an identical lesion.

(Slide) This is the x-ray of a 35-year-old woman who, like the others, had no symptoms. (Slide) It was a unilocular cyst filled with brownish fluid containing many glittering yellow particles. The thymic stroma in its wall was interpreted originally as a degenerating lymphosarcoma. No irradiation was given and she remains well seven and one-half years later.

(Slide) Again a young woman who had no complaints. The preoperative diagnosis was thymoma. (Slide) The specimen was a remarkable, unilocular cyst located in the left lobe of the thymus, the entire gland being seen here. (Slide) On section it was found to contain thick grumous material like that of any cystic terotoid tumor. No doubt it might have been mistaken for a dermoid cyst had not the entire thymus been resected and its relationship thus preserved.

(Slide) This last case, in a middle-aged man, more or less bridges the gap between thymic and dermoid cysts, for the lesion was a classical dermoid cyst containing hair. The wall was comprised of thymic tissue including Hassall's corpuscles. Obviously, a case of this sort goes a long way toward confirming a more than casual relationship between teratoid tumors of the mediastinum and the thymus gland.

DR. PHILIP W. SMITH, Marion, Ohio.—We have studied 32 cases of primary thymic neoplasms of the type described by Dr. Effler. These cases were from the Armed Forces Institute of Pathology and from the University of Michigan. Twelve of these cases had associated myasthenia gravis, 3 had associated Cushing's disease and 17 had no apparent associated neuromuscular or endocrine disorder. Histologically the neoplasms in all three groups were indistinguishable. They are not to be confused with the true lymphomas which may involve the thymus, though at times their histologic morphology is similar enough to make differentiation difficult. A more simplified classification of these neoplasms seems warranted in the light of present knowledge. We believe that the neoplasms in all of the groups described by Dr. Effler have a common cell of origin, the so-called thymic reticulum cell or, perhaps more properly, the thymic syncytial cell. These tumors present a variety of histologic appearances, both between different tumors and in different areas of the same tumor. It is probably superfluous to subclassify them histologically according to their predominant cell pattern because it tells us nothing of their biologic behavior.

We agree that all thymic neoplasms should be considered as actually or potentially malignant. The criteria for malignancy must usually depend on their gross characteristics and upon clinical evaluation of their biologic behavior rather than on histopathologic evidence. Three of these 32 tumors did show regional embolic lymph node metastases. Nearly all showed capsular invasion, and extensive local infiltration and implantation were common.

A prompt tissue diagnosis certainly is essential; and, if possible, total excision of these neoplasms with any remaining thymus should be accomplished. If total excision is not possible, the mediastinal structures often may be mechanically decompressed by removal of a portion of the tumor. Local implantation with appropriate radioactive materials such as iridium and/or externally applied roentgen therapy is definitely indicated if one is not sure that excision is complete. The response of these tumors to irradiation is variable but significantly worth while in a good percentage of them.

Finally, for the sake of the record, the photomicrograph just shown by Dr. Chesney I believe is misclassified as a thymic neoplasm occurring in the lung. A similar tumor is to be found in the files of the Armed Forces Institute of Pathology, also occurring in the lung. I do not believe it is related to the thymus at all but is actually a type of lymphoma. The epithelial-appearing cell clusters are not Hassall's corpuscles but collections of endothelial cells.

DR. DONALD B. EFFLER (Closing).—I want to thank the discussants, and to thank Dr. Meade for closing the discussion before someone less friendly than the others had a chance to speak. I would like to close with the summary which appears in the paper by simply stating that we believe that indications for surgical intervention are the same as in all mediastinal tumors and contraindications are perhaps the same. Tissue diagnosis is mandatory and in all patients, regardless of whether or not the tumor can be removed, a full course of postoperative radiation therapy is recommended.

PULMONARY RESECTION IN ACTIVE CAVITARY (OPEN-POSITIVE) TUBERCULOSIS

ROBERT H. HOLLAND, M.D.* (BY INVITATION), SUNMOUNT, N. Y., JOHN W. BELL, M.D. (BY INVITATION), SUNMOUNT, N. Y., AND EDWARD S. WELLES, M.D., SARANAC LAKE, N. Y.

CURRENT attempts to control cavitary tuberculosis with prolonged chemotherapy result in a predictable incidence of medical failures. For example (Fig. 1), there were no definitive surgical procedures in this random group of 179 original treatment cavitary cases during the first 12 months of chemotherapy with streptomycin and PAS. Following 6 months of drug therapy, 29 per cent had residual cavities and positive sputum, and after 12 months, 18 per cent still had positive sputum and persistent cavities.

In the majority of recent reports,[1-3] no attempt has been made to correlate the preoperative susceptibility of the tubercle bacilli with the postresection complications and therapeutic results. Falk and Tucker[4] state that bacterial resistance to the chemotherapeutic agents at the time of surgery appeared to have little effect upon relapse or failure in their series of resections. Differing from this opinion, we have found this information essential to the proper management of these cases and directly related to the complications and end results.

MATERIAL

This study is a review of 83 sections in 75 patients who had positive sputum and persistent cavities at the time of operation. For convenience in classification, as suggested by Decker, Raleigh, and Welles,[5] the term "open" signifies the persistence of an annular shadow, recognized as such on planigrams. The report of at least one positive sputum culture within the three-month period immediately prior to surgery is sufficient to designate the case as "positive."

Original chemotherapy cases are those in which treatment was started on the first admission, or if on readmission or transfer, not more than 6 months of drug therapy with no interruptions over 2 weeks. All other patients, because of unknown intervals between drug regimens, are considered to be in the re-treatment group.

Further subdivision of the original and re-treatment groups is based on the susceptibility pattern of the tubercle bacilli in the patient, both on the

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admission sputum culture and on the last positive specimen before operation. Susceptible tubercle bacilli are those showing less growth, than in controls, in at least 2 of the 3 tubes of ATS medium containing 15 μg of streptomycin, 10 μg of PAS, and 1 μg of INH per milliliter.

TABLE I. ADMISSION BACTERIAL SUSCEPTIBILITIES

Original Chemotherapy.—	
Susceptible	28
Resistant	0
Re-treatment.—	
Susceptible	42
Resistant	13
	83

On admission (Table I), there were 28 original chemotherapy-susceptible cases, and none were found to be resistant. Forty-two were considered as re-treatment susceptible, and 13 showed resistant bacilli at the beginning of re-treatment. Drug therapy ranged from 2 to 32 months preoperatively, being quite prolonged early in the series in an attempt to convert the sputum.

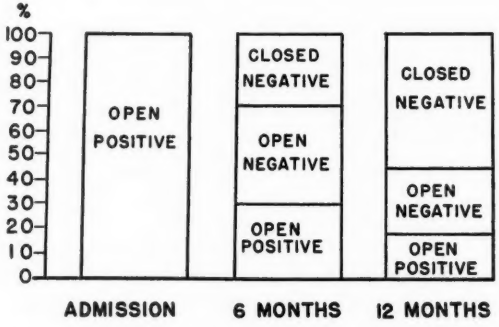

Fig. 1.—Sputum conversion and cavity closure in original chemotherapy.

At the time of operation (Table II), 19 original treatment patients still had susceptible organisms while in 9 the bacilli had become completely resistant. Of the 42 patients re-treated as susceptible, 19 had developed resistant bacilli by the time they were considered for resection of surgery. Thus, a total of 32 patients came to operation in the re-treatment resistant state.

TABLE II. PREOPERATIVE BACTERIAL SUSCEPTIBILITIES

		Net (Change)
Original Chemotherapy.—		
Susceptible	19	↓
Resistant	9	9
Re-treatment Chemotherapy.—		
Susceptible	23	↓
Resistant	32	19

OPERATIVE PROCEDURES

The operations were usually formidable. Nineteen patients had preresection thoracoplasties, 4 had permanent phrenic damage, 2 had Monaldi procedures, 19 had pneumothorax, and 11 were classical thoracoplasty failures. All of these procedures involved the resected side, making the operation more difficult technically, and the postoperative course more complicated physiologically. Wedge resection was performed only twice as a solitary procedure; segmental resection, 44 times; lobectomy, 34 times; and pneumonectomy, 3 times. There were no operative deaths, that is, within 60 days following surgery.

COMPLICATIONS

Major complications of tuberculosis which are defined as bronchopleural fistula, empyema, spread or reactivation of disease, and chest wall infections, are correlated with respect to preoperative susceptibilities of the bacilli in the patient (Fig. 2). In the original chemotherapy-susceptible group, there was 1 major complication in 19 resections, and, in the resistant group, 5 in 9 resections. In the re-treatment susceptible group, there were 3 major complications in 22 resections, and, in the resistant group, 9 in 33 resections. Nine patients in the resistant groups had viomycin and Terramycin added to their chemotherapy protocol 6 weeks prior to operation and were continued on this program at least 8 weeks postoperatively. In this group there were 3 major complications in 9 resections.

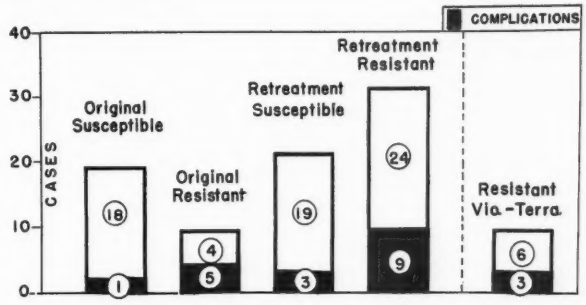

Fig. 2.—Major complications.

THERAPEUTIC RESULTS

Complete follow-up studies on 72 of these 75 patients range from 3 to 52 months, and are again classified in relation to the preoperative bacterial susceptibilities (Table III). Activity is defined as either radiologic or bacteriologic instability within 3 months of this review. In the original treatment-susceptible group, no cases are active, 19 are inactive, and all patients are living; and in the resistant group, 1 case is active, 5 are inactive, and 3 patients are dead. In the re-treatment-susceptible group, 1 case is active, 23 are inactive, and 1 patient died of carcinoma of the tongue with metastases; and in the resistant group, 6 are active, 22 are inactive, and 1 patient is dead.

Of the 9 patients in the resistant groups treated with viomycin and Terramycin, 4 have active cases, 4 inactive, and 1 is dead. Therefore, of the 72 patients followed, 8 have active cases, 64 inactive, and 4 died of tuberculosis which makes a satisfactory arrest rate of 95.5 per cent in the susceptible groups, and 71 per cent in the resistant groups.

TABLE III. CURRENT DISEASE STATUS

	ACTIVE	INACTIVE	DEAD
Original Chemotherapy.—			
Susceptible	0	14	0
Resistant	1	5	3
Re-treatment Chemotherapy.—			
Susceptible	1	18	1*
Resistant	6	22	1
Resistant Viomycin / Terramycin	4	4	1

*Died of cancer of the tongue with metastases.

DISCUSSION

Certain radiologic and bacteriologic findings, which are presented below, have been extremely useful in anticipating medical failures during the early months of chemotherapy.

Radiologic.—

1. Cavity size: 3 cm. or over.

2. Cavity location: (a) extreme apical or posterior; (b) those persisting under a thoracoplasty (Fig. 3, *a*).

3. Cavity configuration: (a) thick-walled, and (b) hanging (Fig. 3, *b*); and (c) stellate (Fig. 3, *c*).

4. Cavity number: multiple adjacent, or those with a honeycomb appearance (Fig. 3, *d*).

5. Cavity with associated bronchial abnormalities: (a) stenosis; (b) ectasia.

Bacteriologic.—

1. Failure to reduce the bacillary content of the sputum in the first 3 months of chemotherapy.

2. Development of partial resistance to streptomycin, PAS, or INH.

3. Failure to convert the sputum in the first 6 months of chemotherapy.

When one or more of these radiologic findings is present, the cavity will usually not close, and when combined with one or more of the bacteriologic findings, sputum conversion is unlikely.

In the candidate for resection who is considered a predictable medical failure, there is little to be gained by prolonging treatment to the point where bacterial resistance emerges. Although the achievement of sputum conversion is desirable, even the open negative state does not guarantee the presence of susceptible bacilli.[6]

Vigilance is particularly necessary in the re-treatment group where the rapid emergence of drug resistance is a common phenomenon.[7] These patients

should be considered for resection several months earlier than their original chemotherapy counterparts and appropriate changes made in their medical protocol if resistance is developing.

The patient with uncertain drug coverage, or known resistance, should be bronchoscoped prior to resection. In these patients, transection of unrecognized endobronchial disease or spillage of tuberculous material at operation may invite pleural complications. The plan at operation in the resistant patient is to perform a wide, clean resection, which usually means a lobectomy,

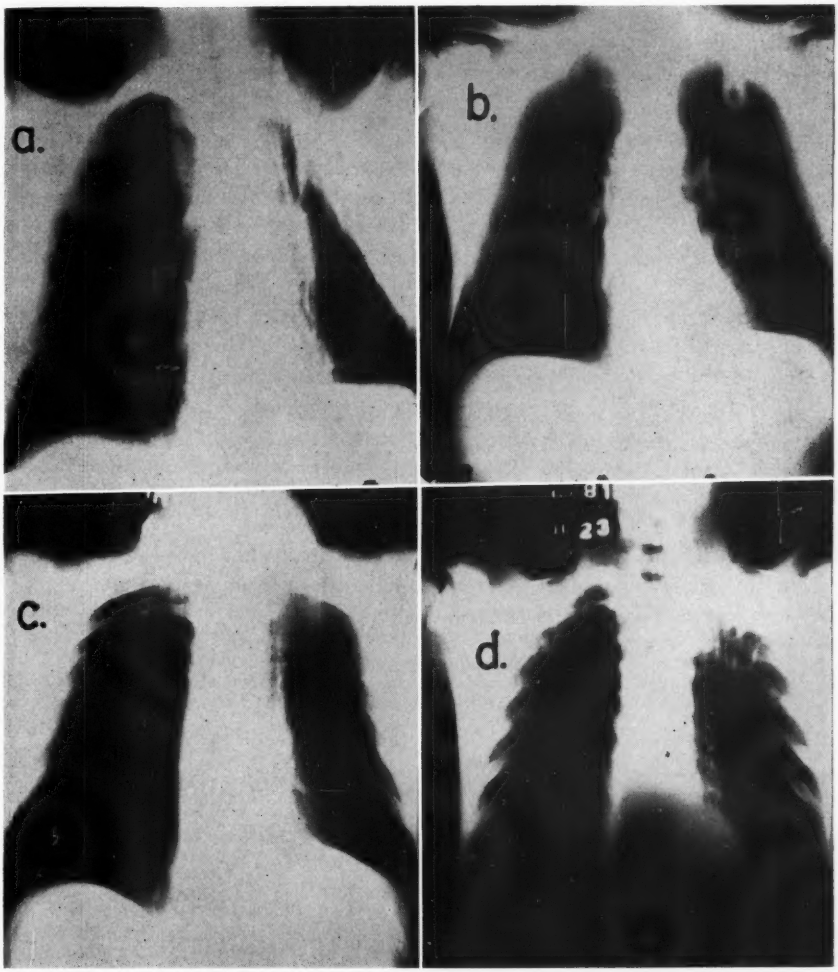

Fig. 3.—Planigrams illustrating various types of cavities that antituberculosis chemotherapy is not likely to close: (*a*) cavity persisting under a thoracoplasty, (*b*) thick-walled and hanging cavity, (*c*) stellate cavity, and (*d*) multiple adjacent cavities.

unless the disease is extremely well circumscribed. This is in contrast to the practice followed in the susceptible group where limited resections have been found to be perfectly safe.

Murphy[8] reports satisfactory results in only 77.6 per cent of his operations for cavitary resection, as compared to 94.7 per cent in those operations where closed lesions were resected. In resections where the sputum was positive, 82.8 per cent of the patients had good results, as compared with 94.4 per cent where it was negative. These statistics are strikingly similar to ours when the bacterial susceptibility data are omitted. Of the three factors, open cavity, positive sputum, and bacterial resistance, we think the latter is the most significant in regard to the postresection complications and therapeutic results.

SUMMARY

1. Eighty-three resections in 75 patients with residual cavities and positive sputum are reviewed. An attempt is made to correlate the preoperative findings on tubercule bacilli susceptibility with the complications and therapeutic results.

2. In the original treatment-susceptible patient, resection should probably be performed between the third and sixth month of chemotherapy, and, in the re-treatment patient, several months earlier in order to avoid the development of bacterial resistance.

3. Of the three factors, open cavity, positive sputum, and bacterial resistance, we believe the latter to be the most significant in regard to the postresection complications and therapeutic results.

4. Despite the presence of open cavity and positive sputum, we have had excellent surgical results in our susceptible patients, and only fair results in those who were resistant.

5. The addition of viomycin and Terramycin to the chemotherapy protocol of 9 resistant patients, 6 weeks preoperatively and continued postoperatively, did not seem to alter the end result.

REFERENCES

1. Douglass, R., Bosworth, E. B., Judd, J. M., and Chang, K. H.: Resection Surgery in Tuberculosis, J. THORACIC SURG. **29**: 136, 1955.
2. Sze, K. C., Sarradi, A., and Conant, J. S.: Pulmonary Resection for Tuberculosis, Am. Rev. Tuberc. **71**: 349, 1955.
3. St. Raymond, A. H., Jr., and Cole, F. H.: Resection for Pulmonary Tuberculosis: A Comparative Study of Segmental Resections and Lobectomies, Ann. Surg. **141**: 87, 1955.
4. Falk, A., and Tucker, W. B.: Resection Failures in Pulmonary Tuberculosis, Tr. Nat. Tuberc. A., 50th Ann. Meeting, 1954, p. 254.
5. Decker, A. M., Jr., Raleigh, J. W., and Welles, E. S.: The Coordination of Surgery and Combined Chemotherapy in the Treatment of Pulmonary Tuberculosis, J. THORACIC SURG. **29**: 151, 1955.
6. Bell, John W.: Unpublished data.
7. Mitchell, R. S.: Early Results of Prolonged Streptomycin-PAS Treatment of Pulmonary Tuberculosis, Ann. Int. Med. **41**: 282, 1954.
8. Murphy, J. D.: A Study of the Factors Influencing the Success of Segmental Resection for Pulmonary Tuberculosis, Tr. Nat. Tuberc. A., 50th Ann. Meeting, 1954, p. 264.

Discussion

DR. WATTS R. WEBB, Sanatorium, Miss.—I want to congratulate this group on their excellent presentation and certainly on some very excellent results in handling a very difficult situation. We have attempted to avoid development of this status, at least in the original treatment group, by the utilization of various teams of the drugs in order that we might always have a group of drugs to which the bacteria presumably would not be resistant. That is, ordinarily we start out with streptomycin and PAS and later on when there appears some evidence of resistance we switch over to isoniazid and Promizole and, later on, as some of the other antibiotics have been developed, we use still a different team. We have on occasion used as many as three teams of antibiotics on a single patient. We feel that this has given us, at least at the time of operation, a team that was effective against the bacteria present at that particular time. In contradistinction to their results we have found that we were thus able to continue effective drug treatment until these patients, judging by the appearance of the contralateral side and other factors, were ready for surgery. Our results in the group that have been treated with various teams of drugs have been superior to those in the group where operation was performed in the pesence of bacterial resistance.

We do concur that an earlier attack on the cavitary lesion is indicated whenever the condition of the remaining lung permits.

DR. WILLIAM M. LEES, Chicago, Ill.—It is encouraging to note that people in the East are also seeing some of these far-advanced and moderately advanced cases that we are seeing in Chicago. This is especially true in view of the fact that a review of the data as recently published in that illustrious journal, the *Chicago Tribune*, has revealed that in some areas of the country the primary indication for surgery is the fact that there are a few flyspecks on the x-ray and an occasional positive sputum; whereas in other parts of the country the large cavities, openly revealed, are permitted to remain, just because the sputum is negative.

In reviewing more than 300 resections during the last 2 years or so, I would like to confirm some of the observations reported by Dr. Holland in that more than 85 per cent of our complications have occurred in those patients with preoperative sputa positive. The majority of these patients have had intermittent chemotherapy, to be sure. However, a number have had continuous chemotherapy, and I think we will find that it is in this group that we are going to encounter most of the complications, at least, from the point of view of the pathology present.

In this group, I am referring to the pathologic specimens which, when studied carefully, will in practically all instances reveal the presence of tuberculous endobronchial disease, not necessarily at the bronchocavitary junction, but at some distance from this area. I believe this plays a considerable role in postoperative complications. We, too, have found that the complication rate is higher in those who have tubercle bacilli resistant to all the drugs. We also attempt to keep viomycin in reserve and we hope that perhaps seromycin, when it becomes available, may be of some benefit in this rather tragic group, small though it is.

DR. FELIX A. HUGHES, JR., Memphis, Tenn.—Thanks to Dr. Barnwell, I have the results of a study of morphology and bacteriology of resected tuberculous lesions in the VA-Army-Navy cooperative study. In my opinion, the data may be said to agree with the recommendation for early surgery. These patients, from 35 hospitals, had operations performed under the supervision of members of this Association.

(slide) This slide shows the percentage of negative lesions, related to the months of chemotherapy treatment, in 494 patients with closed lesions who were clinically negative for acid-fast bacilli. No patients were selected for study with less than 4 months of treatment. Here you can see the bacteriology of the lesions changed very little after 4 to 5 months of chemotherapy. What gain is obtained is accompanied by a gain in positive smears even after 12 months of therapy.

(slide) This slide relates closed lesion bacteriology and chemotherapy regimen to how many months the patients were clinically negative. A gram a day of streptomycin plus PAS administered until the patient was clinically negative for 2 months resulted in excised lesions that showed about as high a percentage of negativity as was found at the end of a year. This confirms, I think, the judgment of the people who resected these lesions, because the lesions showed such a high negative percentage, but it also confirms the observation that as soon as the patient is clinically ready, the resection should be carried out. Even with streptomycin twice a week plus daily PAS, apparently the maximum effect on the lesion is reached after the patient has been clinically negative for 4 to 6 months.

(slide) When considering only patients who had lesions with negative cultures but positive smears, which I think indicates less therapeutic effect than a negative culture with a negative smear, a gram of streptomycin plus PAS daily caused a maximum improvement in the lesion, of being clinically negative, at the end of four months. With streptomycin twice a week plus daily PAS, there is a slight therapeutic increase throughout the 12-month period.

(slide) When it comes to resected open lesions, although still negative clinically, there is a marked decrease in the percentage of lesions that are negative during the period between 4 and 5 months and 6 and 7 months. I think this is very significant and is why the VA studies confirm the recommendations given by Drs. Holland, Bell, and Welles.

This is hindsight evidence, but indicates that astute clinical judgment in the handling of tuberculosis cases is more indicated than ever. From my experience with the resection of approximately 500 tuberculous lesions, I also agree with the recommendations presented here. Our findings have agreed too that when the tubercle bacilli are resistant there is a tremendous increase in the percentage of complications. When there is a predictable medical failure, which frequently can be determined early, resection in suitable patients should be done at the earliest optimum time.

DR. WINFIELD O. KELLEY, Norwich, Conn.—Our findings in the tuberculous cavity are similar to those of Dr. Holland. I would like to stress a point which we feel is very important in evaluating these cases preoperatively. In going through our series of the last 243 cases, I was able to pick out 167 with cavities which perhaps agree with the principles followed by Dr. Holland in his classification. It seems that we are unable to evaluate the cavity situation by regular x-rays alone and we have come to rely upon laminagrams almost exclusively. It has been difficult also, even in that respect because of the interpretation of the roentgenologist and we found we had to include probable cavities even when we used laminagraphic interpretation.

(slide) There were 167 specimens from patients with cavitation; 121 showed acid-fast bacilli by smear or culture, making 72 per cent. There were 104 with a positive smear, at least one positive smear; 90 had positive cultures and only 70 were positive both by smear and culture.

(slide) This may be a more rigid classification than was used by Dr. Holland and his group. For open cavity cases, we specify that the sputum had to be positive within 6 weeks of operation; there was laminagraphic evidence of cavity preoperatively and there was proof that there was a cavity with a positive finding of bacilli in the cavity that had been resected. In this series of 167 specimens from patients with cavitation, there were 121 specimens (72 per cent) which were positive for acid-fast bacilli by smear or culture; 104 (62 per cent) which were positive for acid-fast bacilli at least by smear; 90 (54 per cent) which were positive for acid-fast bacilli at least by culture; and 70 (42 per cent) which were positive for acid-fast bacilli by smear and culture.

The results in these cases were as follows: There were 24 patients whose tests were still positive by smear or culture postoperatively but in 2 of these the organisms proved to be saprophytes. Then we had 22 cases that had to be further evaluated. Most of the specimens became negative soon afterward, the time varying between 1 and 3 months.

Three patients died, not early deaths but late deaths, one of bacterial endocarditis along with advanced tuberculosis; another had far-advanced tuberculosis; the third had an accidental death. One of these patients had a relapse and is now in the hospital.

(slide) In order to point out some of the problems in evaluating these cases, this shows the x-ray after 10 months of streptomycin and PAS therapy. The sputum was positive on admission but became negative and was negative at the time of operation. There is a small lesion in the left lung which is probably impossible for most of you to see. (slide) This is the lesion which was resected.

(slide) There is an obvious cavity here of rather large size, and another smaller lesion here. This patient's specimen was negative by smear but was positive by culture. This case could not be used in our series even though it was proved to be a positive case.

DR. NORMAN J. WILSON, Brookline, Mass.—I should like to compliment Dr. Holland, Dr. Bell, and Dr. Welles, not only for calling our attention to a timely and important subject, but also for calling attention to other important criteria which determine the success of surgical treatment other than those related to drug therapy. We have heard a great deal in the literature, and also here this morning, about drug criteria and the fact that a positive sputum and open cavity are sources of danger to the patient undergoing resection.

I should like to ask, do you really think that is true? Or is it the fact that most patients of this type are those who had the most serious tuberculosis to begin with and those who represent treatment failures? Many patients with open cavities who have been treated over long periods of time, and especially with recurring or persisting positive sputum, have partial to complete resistance. This fact would seem to be of great importance compared with the fact that a positive sputum or an open cavity was present.

Recently Dr. Edward Hayes, Dr. Overholt, and I made a study of a group of patients on their first course of drugs, who had been treated by resection during the early months of treatment. One hundred and eight had resection performed with less than a month of drug therapy. The only difference in statistics in the groups that were studied was that the earlier the resection was done the better the results, provided the surgical criteria were abided by.

What are the surgical criteria? First, that the only threatening lesion is within the unit of lung to be resected and that all other lesions have been controlled by drug therapy and medical treatment. Second, that the patient have an adequate respiratory reserve. Third, that the patient has had intelligent drug treatment sufficient to eliminate toxic symptoms and excessive sputum. It is our experience that when these fundamental surgical criteria are present, the duration of preoperative chemotherapy is unrelated to the results, except that those patients who are operated on very early during the course of drug treatment have slightly better results than those operated on later.

One other thing I would like to pass on: We have found that pyrazinamide is the best drug to protect the patients in serious condition who have already had prolonged chemotherapy while undergoing resection.

DR. A. M. DECKER, Richmond, Va.—I feel an obligation to make two points for the record. First is a point of which Dr. Holland and his colleagues are fully aware, but I am afraid they will perhaps not have time to clarify it directly, and I feel that some of the data might be misinterpreted. The first slide that was presented showed a sharp increase in the per cent of conversion and cavity closure which occurred between 6 and 12 months. Those percentages are correct. However, this is a tapering study with some failures having been removed from the study after 6 months by various means of surgical intervention. So actually the percentage of cavity closure and percentage of failure in the over-all group does not change greatly after 6 months. The other point I would like to make is that we are not yet certain of the exact level of significance of drug resistance. I speak specifically of streptomycin. I think that resistance to 10 μg of streptomycin per cubic centimeter does not correlate with clinical drug resistance as well as resistance to 15 μg. There is certainly a place for further studies along this line.

DR. BELL (Closing).—We are very glad to have had the opportunity of shifting the spotlight to tuberculosis, a disease which the lay press and possibly some physicians seem to believe is no longer a medical problem. Despite the use of all available antituberculosis drugs and modern resection technique, we have been unable to eliminate this disease. You have just heard the morbidity of this chronic relapsing disease. It is still present, and Dr. Medlar has predicted that it will probably increase in coming years.

With regard to Dr. Webb's comment on the various drug combinations by which they have tried to convert these cases to the negative-sputum state, our patients have had a variety of drug combinations, most of which have been continued to the point of resistance rather fruitlessly. In fact, patients who were resistant to streptomycin and PAS will, when isoniazid is added, in effect be getting INH alone and rapidly become resistant to it; thus using one of the best drugs left for surgical coverage. We have not had a great deal of experience with viomycin and Terramycin and Pyrazinamide but as you have seen, the results with viomycin are not encouraging. The number in our series is not great and we obviously do not present this material because we are particularly proud of the results. Nor do we wish to imply that the unsatisfactory cases are necessarily surgical failures; or even just chemotherapeutic failures. Actually, they are probably total failures of both medical and surgical treatment.

We should like to emphasize one point in the current resection surgery of tuberculosis. This is the important consideration of whether or not the surgical candidate is harboring resistant tubercle bacilli. We have just mentioned that late tuberculosis complications occurred in one third of the patients with resistant bacilli who had resections. This incidence is reminiscent of the forbidding morbidity whch occurred in the predrug era. The problem of resistant bacilli is not confined to patients with cavitary disease and positive sputum. We have become aware that even the patient who comes for resection with sputum negative for 3 months or more may harbor, in 10 to 15 per cent of the cases, resistant tubercle bacilli which simply are not being sloughed into the bronchial tree.

In 500 resections at Sunmount Veterans Hospital since 1950, we have had 17 cases of postoperative parenchymal reactivation which have followed at varying intervals after resection. Of these patients, 13 had negative sputum at the time of operation. Two had no cavities, and 11 were operated upon because of the open negative state. The remaining 4 had open cavities and positive sputum. Only 2 of the 17 postresection tuberculosis reactivation cases had susceptible tubercle bacilli. In other words, 15 were resistant. In 10 of the 17 patients, all of whom had both x-ray and bacteriologic relapse, all palpable disease had been removed. The microscopic spillage, which probably occurs in nearly 100 per cent of resections, is apparently innocuous in the patient with good drug control but is not safe in the resistant patient. Segmental resections or wedge resections which open raw surfaces may clear disease by only narrow margins and may also result in transection of unrecognized endobronchial disease at a subsegmental level, as mentioned by Dr. Lees. In view of these facts, we have favored lobectomy in any patient who is suspected of harboring resistant bacilli and who has uncertain drug control, regardless of whether or not the sputum was positive. In 8 patients in whom resistance was not suspected, parenchymal reactivation followed very promptly after segmental excision. Secondary lobectomies were necessary and in 1 case pneumonectomy became necessary to control the disease.

We should like to thank the discussants.

SIMULTANEOUS BILATERAL RESECTION FOR PULMONARY TUBERCULOSIS IN MENTAL PATIENTS

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INTRODUCTION

WHEN in any field of surgery a single operation can successfully replace two operations, an advance has been made. In abdominal surgery staged resections of the colon have been abandoned except when there is obstruction. Only at the beginning were two operations rather than one needed to resect cancer of the pancreas. Excision of cancer of the middle third of the esophagus through the right chest apparently required a two-stage operation at first[14] but it no longer does. It is a surprising anachronism to find recently that a two-stage operation is still recommended for pharyngo-esophageal diverticula[11]; most surgeons gave it up years ago. More examples could be added but the point is clear. One operation is better than two provided, of course, that it accomplishes as much with equivalent risk and disability. This paper describes one way in which a single operative procedure can replace a two-staged operation in the surgery of pulmonary tuberculosis.

Pulmonary tuberculosis frequently spreads bilaterally[15] and it may progress far enough so that a bilateral resection is needed. Conventionally, the disease is excised at two separate operations through two long posterolateral incisions. This is not necessary, for, due to the anatomic distribution of the disease, it is technically quite easy to resect both sides through a single incision. Usually tuberculosis infects the superior poles of the lung and this region, especially, may be reached on both sides through a single, transverse, anterior incision.

It is not difficult to find reasons that favor a simultaneous rather than a staged bilateral resection for selected patients with bilateral disease. The total time of treatment and disability could be shortened and the expense greatly reduced with a single operation. The danger of postoperative aspiration or spread from residual disease is gone if this disease has been taken at the first operation. Then too, respiratory stress may actually be less after a simultaneous bilateral operation than after the second stage of a staged procedure.

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This reasoning might be applied to some of the patients in any tuberculosis sanatorium. Actually, the simultaneous bilateral operation has been done only on the inmates of the Anoka State Mental Hospital and for these particular patients there has been, in our experience, at least one special reason favoring the use of a simultaneous bilateral operation. At the time of writing, 94 patients in the Tuberculosis Unit of the Anoka State Mental Hospital are awaiting surgery. For each of them surgery has been recommended by a joint medical-surgical conference and they are ready, but operating time and facilities are limited and they must wait. With an overwhelming surgical load such as this, a reasonable method of accelerating the care of some patients, such as the simultaneous bilateral resection, seems fully justified.

This long list of patients awaiting surgery reflects merely one facet of a trying problem—tuberculosis in state mental hospitals. The high incidence of the disease in this population is well recognized.[2, 5] The problem has not been solved but at least the management of this situation has been progressive in Minnesota. All mental patients with tuberculosis are isolated in one modern unit which is part of a larger mental hospital. The plan of control and treatment, as well as our experience with resectional surgery in these patients, has been described in another publication.[12] Mental patients with tuberculosis deserve modern care in their own right as ill human beings but they must have it for another reason too. As an important remaining "seed bed" of the disease, they menace the public health.

The history of simultaneous bilateral pulmonary resections is meager. Some possibly apocryphal evidence suggests that one of the first pulmonary resections attempted was actually a bilateral operation done by Block in 1882.[23] It failed. The only medical report, at the time, about this operation was by a correspondent to the *Boston Medical and Surgical Journal* who had not seen the operation.[24] Block himself apparently did not find time to record the case, probably because he was incapacitated with the turmoil that led to his suicide—a direct consequence of his failure. Thus, the operation's history began on a melancholy note.

In recent times Overholt[18] has preceded us. In each of three reported cases, he used a bilateral posterolateral incision to resect segments of both lungs. The disease was bronchiectasis in two cases and the third case was mixed—a tuberculoma was found on one side and a hamartoma on the other. Our first report on the simultaneous bilateral operation was made in 1954.[22]

INDICATIONS

Rather than depend upon antibiotics alone[16] we have preferred, whenever possible, to resect even residual necrotic foci as well as inspissated cavities and more advanced disease.[1, 4, 21] All types of resectional surgery have been used liberally on mental patients with tuberculosis, perhaps even more liberally than resection would have been used for the same stages of disease in sane patients. We have tried to bring each patient to a state of health where he could be removed from the tuberculosis section and returned to the crowded general wards of the mental hospital. This transfer requires caution. In a

state mental hospital tuberculosis is liable to be contagious. Even an infrequent positive sputum arising from an apparently inactive disease can be dangerous if it is produced by an irresponsible patient. Before they leave isolation, patients must show consistently negative gastric cultures and x-rays with no evidence of tuberculosis or, at most, only minimal scarring. In general, then, resection has been recommended for all patients with stable, fibronodular or more advanced disease if the disease appeared to be resectable without undue risk.

The simultaneous bilateral operation has been used for a select fraction of those needing surgery. We have chosen ambulatory patients in relatively good physical health who seemed to require no more than segmental resections on each side. In most cases the gastric cultures were negative and the roentgenologic appearance had been stable for some time. Young patients were preferred. As a matter of fact, however, the patients who had the simultaneous bilateral procedure averaged about the same age as the other surgical patients. No particular psychotic state has contraindicated the operation.

PREOPERATIVE PREPARATION

Preoperative management did not differ from that which preceded unilateral resections. The patients received antibiotics for an average of 12 months (3 to 35 months) before surgery. All had 0.5 Gm. of dihydrostreptomycin twice a week combined with 200 mg. of isoniazid daily. Five patients also took para-aminosalicylic acid during part of their course. Bed rest has proved impractical for most patients with mental disease and so it was not used.

TECHNIQUE OF THE SIMULTANEOUS BILATERAL RESECTION

A Pentothal-curare mixture is used for anesthetic induction and endotracheal intubation with the subsequent addition of nitrous oxide and oxygen in equal parts. In some cases cyclopropane has replaced this mixture during the latter part of the operation. In order to inflate one lung selectively while operating on the other, a double-lumen Carlens' tube[3] was tested; it worked satisfactorily, but is not necessary. Despite the use of controlled respiration throughout with a single-lumen tube, exposure is not obstructed.

The patient lies supine on a roll which elevates the chest (Fig. 1, *A, B, C*) and a transverse anterior incision is made as illustrated in Fig. 1, *A*. In women, the breasts nearly hide the resulting scar. In men, this cosmetic result cannot be achieved so the incision is placed above the nipples. In contrast to a posterolateral incision the muscles of the chest wall beneath this incision suffer little trauma. It is necessary only to split the pectoralis muscles in order to reach the third interspace. This interspace is then opened bilaterally before the sternum is divided transversely. A self-retaining retractor in the midline with another supplementing it on the side under attention provides good exposure (Fig. 1, *D* and *E*). Occasionally the lower sternal segment will press posteriorly against the heart as the wound is opened but this can be corrected by patiently adjusting the position of the retractor blades.

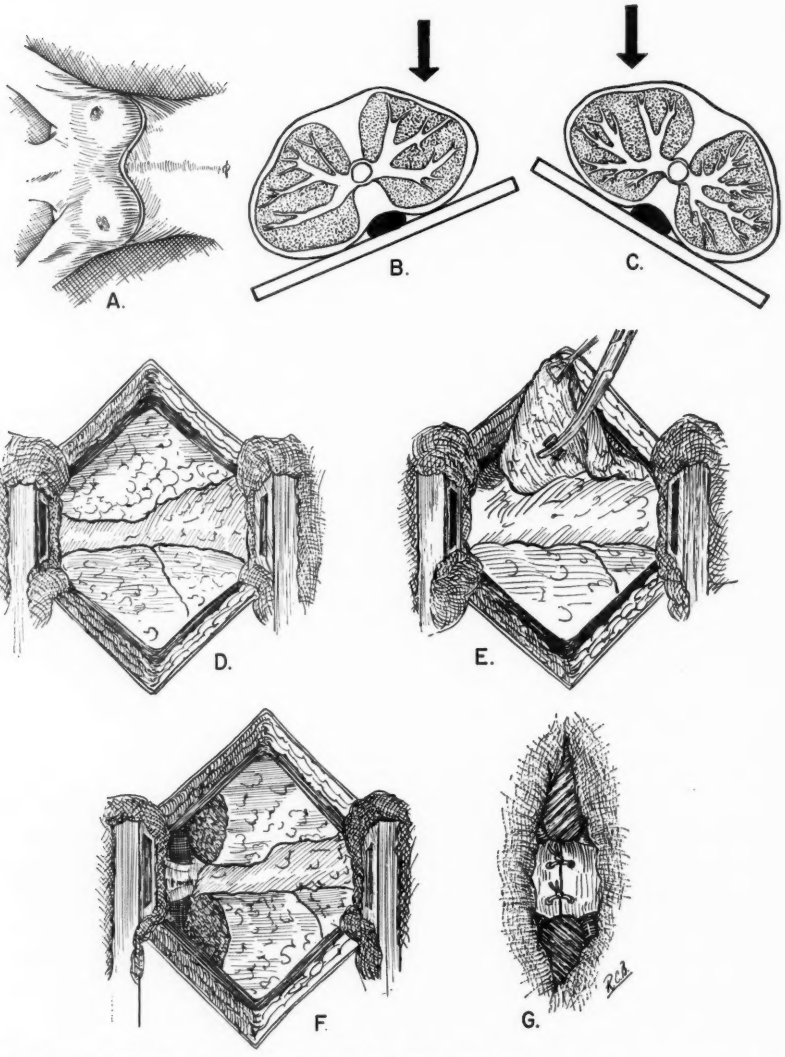

Fig. 1.—Technique of the simultaneous bilateral operation.

A, Position of the patient. The location of the incision in a woman is illustrated. Arms are usually kept at the sides.

B, C, Rotation of the table first to one side and then to the other in order to obtain maximum exposure. A roll of cloth is placed under the back to elevate the center of the chest.

D, Exposure obtained upon opening the wound.

E, Resection of the left apical-posterior segment is in progress. Better exposure is obtained if a second retractor is inserted and if the table is rotated to the patient's right.

F, Resection has been completed on both sides. The raw lung surfaces are illustrated.

G, Sternum approximated with heavy wire sutures.

Resection of both apices can now proceed at the same time with two operating teams but we usually have not had enough help for this. In any case, by doing one side at a time after rotating the table appropriately (Fig. 1, *B* and *C*) a wider field is exposed.

Other authors have described resection techniques in detail[4, 17, 19] so little need be added here. Approach from the front alters none of the essential steps. After cutting the adhesions, we divide the arteries to the diseased segment and then the bronchus. Following this the segment is separated from the rest of the lobe as near as possible to the intersegmental plane, mostly by blunt finger dissection starting from the root. Small veins that cross the intersegmental plane are clamped as they are encountered.

After the resections are completed (Fig. 1, *E*), two large intercostal catheters are fixed in each chest and the wound is closed. The sternum is wired with heavy stainless steel (Fig. 1, *G*) and the muscles are brought together with gut. The entire operation requires but little longer than a unilateral resection because the wound takes less time than a posterolateral wound.

POSTOPERATIVE CARE

Postoperative care demands special vigilance. The mental attitude of the insane always complicates care following any operation and a bilateral thoracotomy obviously adds special hazards. Chest catheters are stitched in place with fishline so that they can be pulled out only with great difficulty and the catheters of each side are connected to separate suction systems. When the lung fails to fill the hemithorax, an additional catheter may be inserted high, anteriorly through a trocar.

Many mental patients do not obey. They may remain passive and indifferent or they may resist treatment actively. In either case, if they do not cough forcefully, a tracheotomy should be made to permit frequent tracheal aspiration.

After recovering from surgery, the patients return to the preoperative routine. Antibiotics are continued for at least four months postoperatively and long enough, in any case, so that a total of twelve months pre- and postoperative treatment has been given. The patients are not kept in bed.

Nine months or more following surgery these patients may be discharged from isolation if they are clinically well, if their x-ray examinations are satisfactory, and if they have had at least 6 negative and no positive gastric culture examinations following discontinuance of antibiotics. Further follow-up conforms to a routine described previously.[12]

CLINICAL MATERIAL

The simultaneous bilateral operation has been done on 16 patients with no deaths. The sex distribution and age range are shown in Table I. The entire group of 187 mental patients who have had pulmonary resections for tuberculosis averaged 46.6 years in age—only a little older than the bilateral group.

TABLE I. SIMULTANEOUS BILATERAL RESECTION FOR PULMONARY TUBERCULOSIS

NUMBER OF PATIENTS	SEX		AVERAGE AGE	AGE RANGE	DEATHS
	M	F			
16	11	5	44	25 to 56	0

One patient was a convict transferred to the tuberculosis unit from prison while the others carried psychiatric diagnoses. Ten had schizophrenia and they were further classified as follows: paranoid, 6, hebephrenic, 3, and catatonic, 1. Three were feeble-minded 1 was a manic depressive, and 1 bore the diagnosis of chronic brain syndrome plus a nonspecified convulsive disorder.

All but one of the operations conformed to our plan of employing the simultaneous bilateral operations for patients who required no more than segmental excisions on each side. The commonest resection, used in 9 patients, was an apical-posterior segmental resection on the left with a resection of both the apical and posterior segments on the right. In 5 patients more lung tissue was removed while in 2, lesser resections proved adequate. Of the 5 in whom more tissue was removed, 2 had the operation just described plus wedge resections of the lingula or superior segment, 1 had the first operation plus resection of the right superior segment, and in 1, resection of the left anterior segment as well as a wedge of the superior segment was added. The fifth had a right upper lobectomy and a wedge resection of the superior segment plus resection of the left apical-posterior segment. One of the 2 patients who required less than the first operation described had an apical-posterior segmental resection on the left but only an apical segmental resection on the right. The other had an apical and posterior segmental resection on the right plus multiple wedge resections on the left.

Ten patients convalesced uneventfully while 6 suffered various significant complications. One man, while unguarded, pulled out all the chest tubes during the first postoperative night and he was, moreover, troubled by retained respiratory secretions. After new tubes were inserted and a tracheotomy was performed he recovered satisfactorily. Two other patients failed to cough effectively and atelectasis developed. Following tracheotomy both of them were relieved of their respiratory difficulty and further trouble was averted.

Finally, the last 3 patients operated upon, all men, have had a complication peculiar to the operative incision used. In each of them the sternal repair broke down. The skin remained intact in 1 and though there was some paradoxical chest motion he was helped by a tracheotomy and maintenance of a flexed posture. He had no further complications. In the second patient the skin separated after the sternum came apart and the wound opening led directly into the superior part of the left pleural cavity. The entire space became infected and in time a bronchopleural fistula appeared. He was treated with a tracheotomy, drainage, and a partial thoracoplasty; the space disappeared and the fistula has finally closed. The last patient in the series also had an anterior wound separation and infection following a sternal breakdown. To begin with, this man was a poor operative risk because he had dif-

fuse, moderately severe pulmonary emphysema and was 52 years old. Despite this trouble he is now recovering rapidly, though the wound is not quite healed. The separated sternum was brought together by keeping him in a sitting position with the thorax flexed. Respirations were further strengthened by using an abdominal binder and by doing a tracheotomy. Fortunately, the pleural cavities were not involved in the wound breakdown.

Since the first of these operations was done only fifteen months ago, its effectiveness in eradicating the disease cannot yet be measured. Up to the present time, however, none of the patients have suffered reactivation of their disease. Four have been discharged from the tuberculosis unit, 1 is awaiting discharge, 5 receive antibiotics no longer and they are undergoing a series of gastric washings for culture examination or await reports on these examinations, and the last 6 patients are still being treated with antibiotics.

DISCUSSION

In our complete series the incidence of bilateral resections, either staged or simultaneous, has been high. Among a total of 187 patients with resections, 26 have had staged bilateral resections and 16 (the present group) have had a simultaneous bilateral operation. Thus 22 per cent of the entire group have had bilateral resections and a few more, still in the unilateral group, may be candidates for a contralateral resection. We have employed resectional surgery freely in this special type of patient—State Mental Hospital inmates with tuberculosis—for reasons discussed earlier in the paper. As a consequence we have apparently found a greater need for bilateral resections than others.[4, 6-10, 20] It is not yet established that residual caseous nodules of tuberculosis should all be resected but at least for our special group of patients we have assumed that this is the best course. If it is, many patients will need bilateral resections and so it is reassuring to know that they can be done with a low risk. Though the fatality rate in the entire group of 187 patients who underwent resection for tuberculosis was 8.6 per cent there were no deaths among the 42 patients who had staged or simultaneous bilateral resections. It must be pointed out, however, that two deaths in the unilateral group were in patients who had anterior incisions similar to the incision used for the bilateral operations. Both succumbed on the thirteenth postoperative day, one of a pulmonary embolism, while the other had bronchopneumonia and atelectasis.

Sternal separation as a postoperative complication was unexpected. A similar sternal repair did not break down in any of the 27 patients whose atrial septal defects were repaired through this type of incision.[13] For the heart operations the sternum was usually divided at the fourth rather than the third interspace and there may be less strain at this lower level, but this seems unlikely. There is another possible explanation. Insane patients often react minimally to painful stimuli and they may, therefore, fail to protect an operative wound as carefully as sane patients do. While agitated, insane patients move strenuously, treating their operative wounds with apparent indifference. Whatever the cause, sternal separation can probably be prevented, even among mentally agitated men, if a stronger sternal repair can be devised.

SUMMARY

1. A simultaneous bilateral resection has been used for pulmonary tuberculosis in 16 inmates of a state mental hospital. There were no deaths.

2. The lungs were exposed through a single anterior, transverse incision with transection of the sternum at the third interspace. Except for the incision, technical details of the resections are those of the conventional operation.

3. Sternal separation postoperatively complicated the recovery of 3 patients.

4. Tuberculosis has not reactivated as yet in any of the patients but the first patient was operated upon only fifteen months ago.

REFERENCES

1. Auerbach, O. Hobby, G. L., Small, M. J., Lenert, T. F., and Comer, J. V.: The Clinicopathologic Significance of the Demonstration of Viable Tubercle Bacilli in Resected Lesions, J. THORACIC SURG. **29**: 109, 1955.
2. Callahan, F. F.: The Present Status of Tuberculosis in Minnesota. Beginning of Tuberculosis Control. A Preliminary Report, Minnesota Med. **36**: 33, 1953.
3. Carlens, E.: A New Flexible Double-Lumen Catheter for Bronchospirometry, J. THORACIC SURG. **18**: 742, 1949.
4. Chamberlain, J. M., Storey, C. F., Klopstock, R., and Daniels, C. F.: Segmental Resection for Pulmonary Tuberculosis (300 Cases, J. THORACIC SURG. **26**: 471, 1953.
5. Committee on Hospitals of the Group for the Advancement of Psychiatry: Control and Treatment of Tuberculosis in Mental Hospitals, Report No. 24, January, 1954, pp. 16.
6. Davidson, L. R., Alexander, H., Lustig, G. J., Kesner, B. J., Stern, S., and Bloomberg, A. E.: An Analytic Review of Excisional Surgery for Pulmonary Tuberculosis, Dis. Chest **25**: 1, 1954.
7. Douglass, R., Bosworth, E. B., Judd, J. M., and Chang, K. H.: Resection Surgery in Tuberculosis, J. THORACIC SURG. **29**: 136, 1955.
8. Forsee, J. H.: The Surgery of Pulmonary Tuberculosis, Philadelphia, 1954, Lea & Febiger, p. 208.
9. Gale, J. W., Dickie, H. A., and Curreri, A. R.: Pulmonary Resection in Tuberculosis, Ann. Surg. **136**: 132, 1952.
10. Kelley, W. O., and Pecora, D. V.: Resection in Pulmonary Tuberculosis. Analysis of One Hundred Seven Operations on One Hundred One Patients, With Early Results, J. THORACIC SURG. **24**: 510, 1952.
11. Lahey, F. H., and Warren, K. W.: Esophageal Diverticula, Surg., Gynec. & Obst. **98**: 1, 1954.
12. Lewis, F. J., Perry, J. F., Jr., Zimmermann, B., Connolly, C. J., Jr., and Callahan, F. F.: Pulmonary Resection in Mental Patients With Tuberculosis, Dis. Chest **27**: 563, 1955.
13. Lewis, F. J., Taufic, M., Varco, R. L., and Niazi, S.: The Surgical Anatomy of Atrial Septal Defects. Experiences With Repair Under Direct Vision, Ann. Surg. **142**: 401, 1955.
14. Lewis, I.: The Surgical Treatment of Carcinoma of the Oesophagus With Special Reference to a New Operation for Growths of the Middle Third, Brit. J. Surg. **34**: 18, 1946.
15. Myers, J. A.: Tuberculosis Among Children and Adults, ed. 3, Springfield, Ill., 1951, Charles C Thomas, Publisher, p. 894.
16. O'Brien, E. J., Miller, A. C., Chapman, P. T., Koster, K., and O'Rourke, P. V.: The Present Chaos Regarding Resection of Residual Caseous Lesions in Pulmonary Tuberculosis, J. THORACIC SURG. **26**: 441, 1953.
17. Overholt, R. H., and Langer, L.: The Technic of Pulmonary Resection, Springfield, Ill., 1949, Charles C Thomas, Publisher, p. 193.
18. Overholt, R. H., Rheinlander, F. H., and Bolton, H. E.: Simultaneous Bilateral Pulmonary Segmental Resection, Bull. New England M. Center **14**: 1, 1952.
19. Ramsay, B. H.: The Anatomic Guide to the Intersegmental Plane, Surgery **25**: 533, 1949.
20. Raymond, A. H., Jr., and Cole, F. H.: Resection for Pulmonary Tuberculosis, A Comparative Study of Segmental Resections and Lobectomies, Ann. Surg. **141**: 87, 1955.

21. Ryan, B. J., Medlar, E. M., and Welles, E. S.: Simple Excision in the Treatment of Pulmonary Tuberculosis, J. THORACIC SURG. **23**: 327, 1952.
22. Shumway, N. E., Lewis, F. J., Zimmermann, B., and Weatherhead, D. S. P.: Staged and Simultaneous Bilateral Pulmonary Resection for Tuberculosis, J. THORACIC SURG. **28**: 90, 1954.
23. Thornton, T. F., Jr., and Adams, W. E.: The Resection of Lung Tissue for Pulmonary Tuberculosis, Internat. Abstr. Surg. **75**: 312, 1942.
24. Walton, G. L.: Letter From Berlin to the Editor, Boston M. & S. J., **108**: 261, 1883.

DISCUSSION

DR. RICHARD H. MEADE, Grand Rapids, Mich.—I rise not to discuss the merits of this paper, which I think is an excellent presentation, but I want to be the first to say that I think this is the best presentation we have had. Here is a man who has talked to you, who has not read a paper. I hope the time will come when this organization can have all papers presented in this manner.

DR. G. N. J. SOMMER, Jr., Trenton, N. J.—I think it is a very wonderful thing to have this subject—the treatment of tuberculosis in the mentally ill—discussed before this Association. We all know it is a serious problem that is very much neglected. I believe it is a problem that can be solved. The solution will come through a treatment program in every mental hospital and by a very careful program of detection. I am rather surprised to read that, in New York State, the mental institutions have had four or five surveys in the last seven or eight years. I believe it is important that a survey of all the patients and employees be done twice a year in each hospital. In our own experience in the State Hospital at Trenton, we have, I believe, cut down our incidence of new cases developing among our own patients tremendously by this program, and by proper isolation of the patients. A great many of our patients with severe tuberculosis are now admitted from the outside rather than developing tuberculosis within the institution.

To get down to Dr. Lewis' paper, I am much impressed by the total number of patients operated upon. I am not surprised in this particular operation of bilateral resection that the three most serious complications occurred in the last 3 patients. That has been my experience. About the time I thought that I could get as good results generally with psychotic patients as with nonpsychotic patients, I ran into trouble. Quite frankly, I am not in sympathy with the bilateral operation, because I have an idea that if he continues he is going to have a greater percentage of serious complications than he thought he would have in the beginning. The last 3 patients were those who had sternal separations.

In my own experience these are difficult patients to operate upon. That does not deter me and I hope it does not deter any others, but one is certainly going to have more trouble. I have had enough trouble with unilateral operations without going into bilateral operations at one sitting. As Dr. Lewis pointed out, the average age of these patients is higher than in nonpsychotic patients upon whom we all operate. I have the feeling that we could go back in some of these patients and do thoracoplasties, because in the older group we find more serious emphysema. This is my experience, and in talking to some of the members of this Association I understand they have had similar troubles; it leads to more difficulty with air leaks and eventually with bronchial fistulas from the unexpanded lung. For those patients, I have an idea that thoracoplasty offers a safer method of operation.

Several years ago, with my colleagues in two hospitals, we reported a number of cases of thoracoplasties with good early results. These results have stood up very well, and I believe that this is an indication that in a number of older patients we should go back to this procedure, once so popular.

DR. RICHARD H. OVERHOLT, Boston, Mass.—Since one is often confronted with the problem of bilateral surgical disease, it is fortunate that we have heard this presenta-

tion today. It may be unfortunate that there are not psychiatrists present so that they might hear of a new type of shock therapy. There is no question but that certain patients with bilateral pulmonary disease may be saved time, money, and considerable discomfort if a bilateral procedure can be accomplished at one sitting. Dr. Lewis and his group have been confronted with a captive group of patients. Our experience has been with patients who voluntarily elect to come. This has forced us to be deeply concerned with morbidity, mortality, complications, total discomfort, and expense.

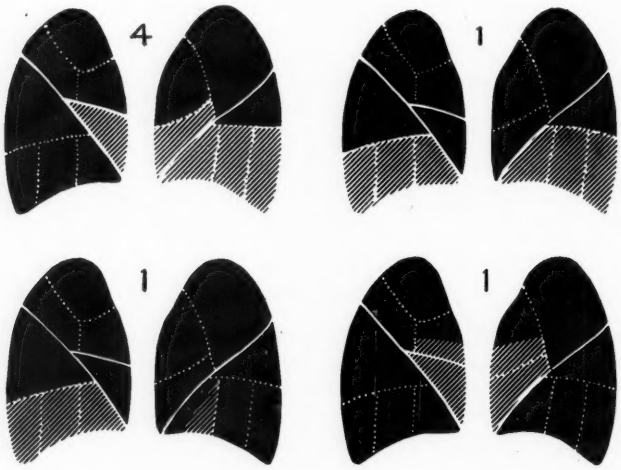

Fig. 1.—Simultaneous bilateral resection—bronchiectasis.

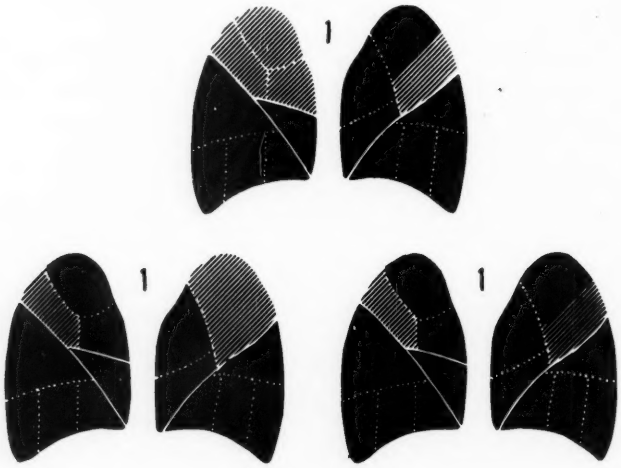

Fig. 2.—Simultaneous bilateral resection—tuberculosis.

SIMULTANEOUS BILATERAL RESECTION

Total 10

DATE	DIAGNOSIS	NUMBER
1952	Bronchiectasis	3
	Tuberculosis tumor	1
1953	Bronchiectasis	1
	Tuberculosis	2
1954	Bronchiectasis	2
1955	Bronchiectasis	1

Our first operation was performed in January, 1952. This was for bronchiectasis involving both right and left anterior segments, the middle lobe and the lingula.

The extent of the resection in the 7 bronchiectasis cases is shown. Four cases had an identical pattern. In this group, we elected to do the right side first and then, if everything went well, we proceeded immediately with the second, or left side.

The extent of resection in the 3 cases treated by simultaneous resection for tuberculosis is shown. The patient in whom only the posterior segments required removal was a young patient with diabetes which was difficult to control. She was four months pregnant. There was active cavitary disease. The direct approach appeared to be the surest, safest, and quickest way to control the tuberculous complicating factor.

SIMULTANEOUS BILATERAL RESECTION

Total 10

Mortality		0
Morbidity	P. O. hospital stay	
Average	15 days	
Longest	26 days*	
Shortest	10 days	

There was no mortality and the hospital stay was not significantly longer than for patients undergoing unilateral surgery.

Dr. Lewis has advised an anterior approach with a division of the sternum. There are reasons why I would not use this method. In the first place, both cavities are opened in the beginning before it can be decided whether or not it is wise to proceed with both resections simultaneously. Second, it is safer to have one side sealed before opening the contralateral cavity. Third, the division of the sternum is accompanied by more interference with costal-cage action and more pain postoperatively than is found with two independent posterolateral wounds.

DR. JOHN PETTER, Rutland Heights, Mass.—The possible advantages of simultaneous resection, particularly in mental patients, are recognized. We believe, however, that the added risk of simultaneous bilateral complications makes staging of the procedures a safer program for the average patient. Our reasons for adopting a more conservative program are as follows:

1. Studies in our laboratory and in others have shown that although the loss of function following resection of up to five segments is usually very small, this loss may be significantly greater if pleural or bronchial complications develop.

2. These complications, though infrequent in well selected cases, remain unpredictable in any individual case.

3. In the event of a significant functional loss following the first resection, interval pulmonary function studies may prove helpful in deciding whether or not the contralateral resection may be safely undertaken. If not, the original plan may be changed, either in selection of a procedure with lower risk of added function loss, or no further surgery.

4. The loss of time by staging the second procedure rarely exceeds two months.

5. Further resolution of the remaining disease after the first resection may preclude the need for a second operation.

*Only 1 complication—empyema.

(slide) I would like to present briefly our series of 32 patients who have had staged bilateral surgery at Rutland Heights Veterans Administration Hospital. Twelve patients had bilateral resection, 10 had bilateral thoracoplasty, 9 had resection on one side, thoracoplasty on the other, and 1 patient had decortication followed later by contralateral thoracoplasty. Complete pulmonary function studies were performed on all patients prior to operation on the contralateral side.

(slide) There were no operative deaths and no late deaths due to tuberculosis. Two patients, both with bilateral thoracoplasties, have died at home of nontuberculous causes three years after the second operation. All patients have been followed to date. There are no pulmonary cripples. Twenty-one are at home with negative sputum, one positive. Eight patients recently operated upon are still hospitalized, six negative, two positive.

In summary, we agree that bilateral surgery should be performed when necessary, but we believe that even in carefully selected cases, staging of the procedures with interval pulmonary function studies is a safer and more widely applicable policy.

DR. DENTON A. COOLEY, Houston, Texas.—I congratulate Dr. Lewis on a most interesting paper which poses many fascinating and challenging problems. We have used bilateral simultaneous thoracotomy in patients with recurrent spontaneous pneumothorax occurring bilaterally. It is well known that anterior intercostal incisions provide adequate exposure for pulmonary resections without transecting the sternum. Failure of sternal healing could be a serious complication and one which in this case is avoidable without interfering appreciably with the surgical exposure by employing separate incisions.

DR. LAURENCE H. RUBENSTEIN, Chicago, Ill.—I wish to congratulate the authors on their bold attack on tuberculosis control in mental institutions. In the State of Illinois Mental Hospitals (Kankakee State Hospital), we also feel strongly about surgical treatment for tuberculosis in the mental patient and have embarked on a surgical program. While we have not done simultaneous bilateral resections we have encountered every type of surgical problem and have been pleased with the success of such a program. In more than 150 cases we have had no deaths. In order to eradicate and control tuberculosis in mental institutions we feel an energetic surgical program must be instituted.

DR. LEWIS (Closing).—I should like to thank the discussants for their kind and generally tolerant remarks. I expected a good deal of trouble, actually. I appreciate Dr. Cooley's suggestion about using the anterior approach for other types of lung surgery. We have considered it but have not had suitable cases. I would like to point out that that incision would probably not be as suitable for lower lung resections, the type Dr. Overholt has done through two incisions, because the heart, especially on the left side, seems to obstruct a good view of the lower part of the lung root.

I cannot reply to all the suggestions or answer all the implied criticisms. We have not had the facilities for doing lung function studies on these cases, but I do feel that the anterior incision actually, if the sternum does not separate, is a much easier incision to bear than a one-sided posterolateral incision.

BLOOD VOLUME STUDIES IN PULMONARY TUBERCULOSIS

An Analysis of 100 Cases

John H. Kehne, M.D. (by invitation), Felix A. Hughes, M.D., and Frank S. Schlenker, Ph.D. (by invitation)
Memphis, Tenn.

THE importance of blood volume deficiencies in the chronically ill patient has been stressed in previously published reports[1-5] but limited observations have been made in patients who have chronic pulmonary tuberculosis.[6] Despite general knowledge of the problem, designated by Clark and associates[1] as chronic shock, patients with chronic pulmonary tuberculosis continue to be transferred to the Thoracic Surgical Section of the Veterans Administration Medical Teaching Group Hospital (Kennedy) who, despite long periods of hospitalization and treatment, present clinical manifestations of blood volume deficiency. These symptoms commonly occur in patients with pulmonary tuberculosis, but are usually interpreted as manifestations of the underlying pulmonary disease. A survey study of blood volume was undertaken to determine the frequency and magnitude of the existing deficiencies. The present report is an evaluation of the blood volume studies in 100 unselected patients with pulmonary tuberculosis who were considered candidates for thoracic surgical procedures.

METHOD

Plasma volume was determined by the Evans blue dye method as described by Gregersen[7] and modified by Gibson and Evelyn[8] for the photoelectric colorimeter.

Hematocrit values were determined by the Wintrobe method and utilized in calculating the total blood volume. The normal expected values for blood and plasma volumes were found by multiplying the normal average pre-illness weight expressed in kilograms by 85 ml. per kilogram and 45 ml. per kilogram for blood and plasma volumes respectively.[8] In the group of patients in whom obesity was a factor, prior to illness, the ideal weight based upon the standard weight tables for sex, age, and height were used.[1] Total hemoglobin mass was determined by the formula

$$\frac{\text{Total blood volume} \times \text{Hgb./100 c.c.}}{100}.$$

Deficiencies for blood volume, plasma volume, and total hemoglobin mass were determined by subtracting the calculated values from the expected values based upon the normal or ideal weight.

From the Thoracic Surgical and Laboratory Services, Veterans Administration Medical Teaching Group Hospital, Memphis 15, Tenn.

Read at the Thirty-fifth Annual Meeting of The American Association for Thoracic Surgery at Atlantic City, N. J., April 24 to 26, 1955.

CASE ANALYSIS

The patients included in the surveyed groups varied in age from 21 to 64 years. All patients had an established diagnosis of pulmonary tuberculosis varying from one to twelve years and had periods of continuous hospitalization varying from nine months to four years prior to the blood volume studies. These patients were transferred to the Thoracic Surgical Section of Kennedy Hospital from pulmonary disease sections of five hospitals in the South. Selection was made from consecutive admissions of patients who were considered to be candidates for either resectional or collapse therapy as an adjunct to their course of tuberculosis treatment.

RESULTS

In Table I are presented the mean values for blood and plasma volume and total hemoglobin mass for a group of 25 normal male adults, and 100 patients with chronic pulmonary tuberculosis considered to be candidates for thoracic surgical therapy. Blood and plasma volumes are expressed in terms of cubic centimeters per square meter of body surface and total hemoglobin mass in grams per square meter of body surface. The 100 tuberculous patients were subdivided into two groups: (a) 38 patients who were found to have no significant deficit in blood or plasma volume and hemoglobin mass, and (b) 62 patients who had significant deficits. Deficiencies of less than 500 c.c. of whole blood were considered to be within the limits of laboratory error and were included with the nondeficient group.

TABLE I. BLOOD AND PLASMA VOLUME DETERMINATIONS

GROUP	NO.	MEAN BLOOD VOLUME C.C./SQ.M.	MEAN PLASMA VOLUME C.C./SQ.M.	MEAN HEMOGLOBIN MASS GM./SQ.M.
I. Normal adult	25	2971	1690	447
II. Tuberculosis	100			
normal—Group A	38	3064	1668	466
deficient—Group B	62	2710	1532	379
Group difference (A – B)		354	136	87

Blood Volume.—The mean blood volume for the normal-control group was found to be 2,971 c.c. per square meter body surface and 3,064 c.c. per square meter body surface for the tuberculosis group (A) which was normal in volume (Table I). The difference is not statistically significant. The mean blood volume for the deficient tuberculosis group (B) was 2,710 c.c. per square meter body surface, a group difference (A minus B) of 354 c.c. per square meter body surface. Although numerically small, this value was an average deficiency of 12 per cent in total blood volume.

Plasma Volume.—Comparable mean plasma volumes were found for the normal-control group and the nondeficient tuberculosis group (A), the values being 1,690 c.c. per square meter body surface and 1,668 c.c. per square meter body surface, respectively (Table I). In the deficient group (B), the mean plasma volume was found to be 1,532 c.c. per square meter body surface, repre-

senting an average group difference (A minus B) of 136 c.c. per square meter body surface or 8 per cent average plasma volume deficiency (Table I).

The mean values for both blood and plasma volume have been presented graphically in Fig. 1. It is to be noted that the mean values for the normal-control group and nondeficient tuberculosis group are comparable. In the deficient group, however, it can be seen that the decrease in blood volume has exceeded the fall in plasma volume and represents a relative increase in plasma volume of 4 per cent. In no case was the laboratory value for plasma volume found to exceed the calculated plasma volume, and attempts to correlate either blood or plasma volume with disease activity or nutritional status were unsuccessful.

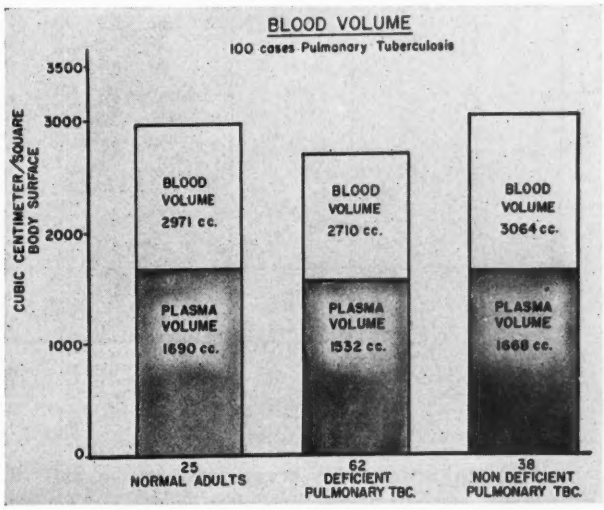

Fig. 1.

Total Hemoglobin Mass.—Comparison of the mean hemoglobin mass for the normal-control group (447 Gm. per square meter body surface) and the nondeficient tuberculosis group (466 Gm. per square meter body surface) reveals no significant difference (Table I). The average deficiency in total hemoglobin mass for the deficient tuberculosis group was 87 Gm. per square meter body surface or an average deficiency of 19 per cent.

The values obtained for total hemoglobin mass have been presented graphically in Fig. 2 for the 100 cases of pulmonary tuberculosis. The deficient group of 62 cases was further subdivided into Group A, deficient by calculation but without excessive weight loss and only moderate pulmonary involvement, and Group B with weight losses in excess of 20 per cent body weight or with more extensive pulmonary involvement than was seen in Group A. The mean hemoglobin mass for the entire group of 62 cases found to be deficient was 379 Gm. per square meter body surface (Fig. 2). Thirty-one cases

could be classified in Group A with an average total hemoglobin mass of 378 Gm. per square meter body surface and 31 cases in Group B with an average hemoglobin mass of 381 Gm. per square meter body surface. Although the major individual case deficiencies in total hemoglobin mass were found in Group B, this is not apparent from the average values, indicating either a considerable group variation or a poor correlation with surface area.

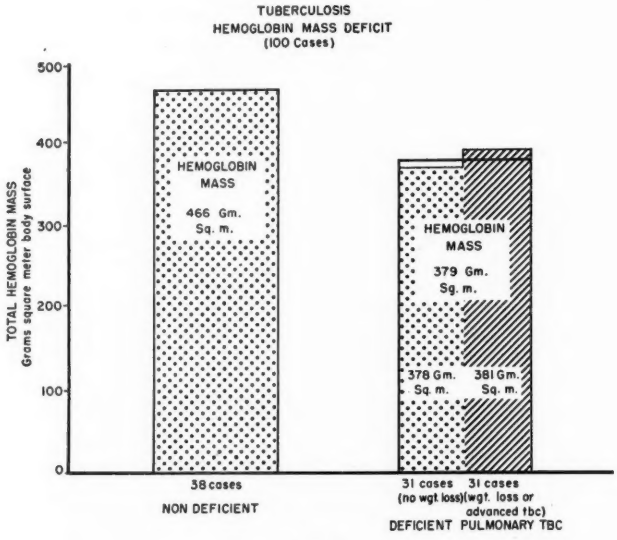

Fig. 2.

Inasmuch as the major deficiency between the normal-control group and the deficient tuberculosis group was in total hemoglobin mass with an average deficiency of 19 per cent, this value was selected for further analysis. In view of the average decrease in blood volume of 12 per cent in the deficient tuberculous group, it is apparent that total hemoglobin mass replacement would be limited by the deficiency in total blood volume. Therefore, replacement therapy should consist of both whole citrated blood and washed red blood cells suspended in isotonic saline solution.

Fig. 3 presents the hemoglobin mass requirements for the 100 tuberculous patients included in this study. The deficiency is expressed in the hemoglobin equivalent of 500 c.c. of blood (15 Gm. hemoglobin equivalent to 100 c.c. whole blood). Sixteen patients required the hemoglobin equivalent of 500 c.c. of whole blood; 23 patients required 1,000 c.c.; 15 required 1,500 c.c.; 5 patients 2,000 c.c.; and 3 required 2,500 c.c. In summation, 62 per cent of the 100 patients required the hemoglobin equivalent of 500 c.c. or more of blood; 46 per cent required 1,000 c.c. or more; 23 per cent required 1,500 c.c. or more; and 8 per cent required 2,000 c.c. or more.

In each of the 38 cases included in the nondeficient group (A) the hemogram was normal. In the 62 cases with blood volume deficiencies (Group B),

normal values for red-cell count, hemoglobin, and hematocrit were reported in 50 per cent, and the remaining 50 per cent were below the expected normal values. The reported laboratory values in general failed to reflect the degree of deficiency either in blood volume or hemoglobin mass. The variation in blood volume and plasma volume seen in Fig. 1 has been described elsewhere[1, 6, 9] and explains why routine laboratory values misrepresent the true hematologic status.

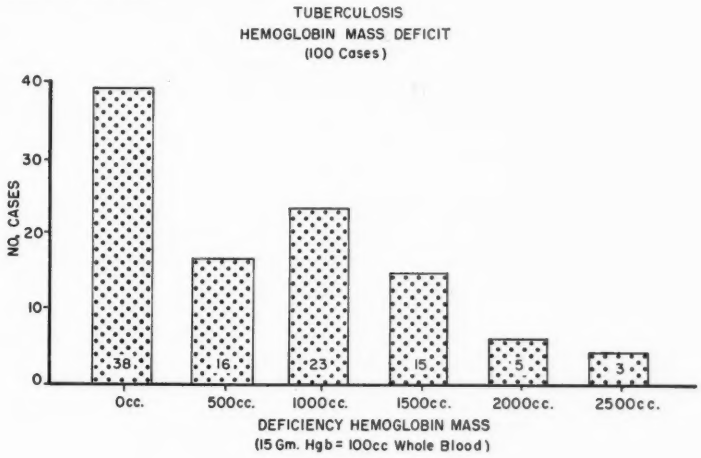

Fig. 3.

It has been reported[1] that a clinical history of weight loss has consistently indicated a reduction in blood volume and total circulating hemoglobin mass. The grouping of the 38 cases of tuberculosis with normal blood volume and 62 cases deficient in blood volume with reference to weight loss is shown in Table II. There were 12 cases (32 per cent) in which the recorded weight loss was 10 per cent or more in the nondeficient group and 23 cases (37 per cent) in which the weight losses were 10 per cent or more in the deficient group.

TABLE II. PULMONARY TUBERCULOSIS (100 CASES)

WEIGHT LOSS	0%	10%	20%	30%	40%
Normal blood volume	26	7	5	0	0
Deficient blood volume	39	9	12	1	1

However, the major portion of these was in excess of 20 per cent total weight loss. It is apparent that weight loss fails to identify the patient with a blood volume deficiency, but when a major weight loss is present a deficiency must be suspected.

CASE REPORTS

CASE 1.—A 27-year-old white man had had a diagnosis of pulmonary tuberculosis since October, 1952. His height was 68 inches; average normal weight, 125 pounds. Initial therapy consisted of bed rest, streptomycin and isoniazid in combination with para-aminosalicylic acid. The sputum was persistently positive for acid-fast bacilli. On Feb. 3, 1953,

right decortication and upper lobectomy were performed. The postoperative course was complicated by a persistent bronchopleural fistula which was controlled by a right 5-rib thoracoplasty on Feb. 20, 1953; modified Schede thoracoplasty on March 13, 1953, and final revision thoracoplasty on April 27, 1953. During this period of treatment, a weight loss of 19 pounds was recorded. At the time of transfer to another hospital for continued treatment, hemoglobin was reported as 11.8 Gm./100 c.c. During the ensuing two months, he failed to gain weight and hemoglobin values of 11 to 12 Gm./100 c.c. were recorded. No effort was made to correct his deficiency. He was returned to Kennedy Hospital for treatment of right costal-arch chondritis and draining sinus on July 20, 1953. The sputum had remained negative for acid-fast bacilli after the lobectomy.

Examination revealed a pale, apathetic, white man appearing chronically ill. The superficial veins of the extremities were collapsed. It was noted that he spent much of his time in bed and his appetite was poor.

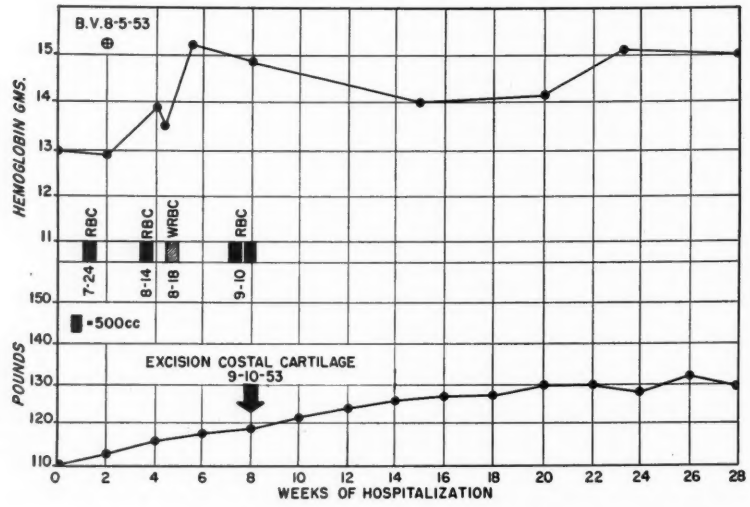

Fig. 4.

Laboratory Data (July 21, 1953).—Red-cell count, 4.9 million; hemoglobin, 13 Gm.; hematocrit, 43 mm. Because of these findings, an initial transfusion of 500 c.c. of whole blood was given after which blood volume studies were done using the T-1824 or Evans blue dye method. A residual deficiency of 573 c.c. or 16 per cent in blood volume was found and a deficiency of 192 Gm. of hemoglobin or 24 per cent of the expected hemoglobin mass. He was given 500 c.c. of whole blood and 500 c.c. of washed red blood cells suspended in saline solution. The weight-laboratory correlation is recorded in Fig. 4. There was an immediate return of appetite, requiring an increase in caloric intake to 5,000 calories, and a progressive weight gain became apparent. He became jovial, ambitious, and overly active, making enforcement of the rest requirement difficult. Surgery was performed for the correction of the osteochondritis and chronic draining sinus; and at the time of discharge on Jan. 15, 1954, he had regained 21 pounds in weight.

Comment.—This patient had developed an accumulative blood volume deficiency following a series of operations for removal of the right upper lobe of the lung and control of a complicating bronchopleural fistula. Satisfactory

restoration of blood volume had never been accomplished. Despite consistently negative sputum following the initial procedure, the manifestations of a blood volume deficiency persisted, i.e., pallor, superficial venous collapse, apathy, anorexia, lack of enthusiasm and energy, easy fatigability, and inability to regain a major weight loss. It is possible that with the passage of time the deficiency would have been corrected, but it is apparent from our observations that the patient's clinical course was rapidly reversed by volumetric blood volume replacement.

CASE 2.—A 28-year-old Negro man was admitted on Sept. 6, 1951, following six months of bed rest for diagnosed pulmonary tuberculosis. X-ray examination of the chest revealed far-advanced involvement of both lungs. The sputum was positive for acid-fast bacilli. Laboratory work at the time of admission: red-cell count, 2.3 million; hemoglobin, 6.9 Gm. The patient received streptomycin, 1 Gm. daily; PAS, 12 Gm. daily; and Chloromycetin, 1 Gm. daily. He was given 1,000 c.c. of citrated blood. Thereafter, he developed resistance to streptomycin and PAS and was given subsequent courses of aldinamide, INH, and viomycin. Resistance developed to all drugs with the exception of viomycin. Bronchoscopy was performed which revealed a profuse mucopurulent bronchial secretion and acute inflammatory changes involving the left main bronchus. The patient remained seriously ill and developed a psychosis manifested by a fetal position in bed accompanied by speech and thought impairment. His general condition thereafter slowly improved. The sputum remained positive for acid-fast bacilli by smear and culture. During the period of acute illness, he developed flexion contractures of both knees which were partially corrected by active and passive exercises and the use of plaster splints. He had been completely bedfast for approximately one year prior to the time of transfer to the Thoracic Surgical Section on Jan. 8, 1954. At that time, examination revealed a mentally dull, apathetic, Negro man with evidence of marked muscular wasting. There were pallor of the conjunctiva and mucous membranes and evidence of peripheral superficial venous collapse. It was estimated that his weight was approximately 100 pounds in contrast to his normal weight of 160 pounds. X-ray examination of the chest revealed far-advanced bilateral tuberculosis with extensive cavitation of the left upper lobe.

Laboratory Data (Jan. 8, 1954).—Red-cell count, 4.22 million; hemoglobin, 11.4 Gm.; hematocrit, 37 mm.; sedimentation rate, 34 mm. per hour corrected. A blood volume determination was performed on Feb. 10, 1954, utilizing the T-1824 method and the following deficiencies calculated: total blood volume, 993 c.c. or 16 per cent of normal; plasma volume, 210 c.c. or 6 per cent of normal; total hemoglobin mass, 269 Gm. or 28 per cent of normal. It was estimated that blood replacement requirements would be 500 ml. of whole blood plus 1,500 ml. of washed red blood cells suspended in normal saline solution.

Transfusions of 500 c.c. of citrated blood were given on Feb. 12, 1954, and on Feb. 15, 1954, followed by a total of 1,500 c.c. of washed red blood cells.

After the final transfusion, the following laboratory reports were recorded: red-cell count, 5.9 million; hemoglobin, 15.6 Gm.; hematocrit, 49 mm. The patient became mentally alert, physically stronger, and he required a 5,000 calorie diet as his appetite improved remarkably. He was able to sit in a wheelchair daily for increasing periods. A progressive weight gain was noted for the first time. It was possible to perform a left anterior-stage thoracoplasty on Feb. 18, 1954; first-stage posterior thoracoplasty on March 15, 1954; second-stage posterior thoracoplasty on April 20, 1954; and third-stage posterior thoracoplasty on May 18, 1954. Adequate blood transfusion replacements were given during each operative procedure and all procedures were tolerated well. The sputum remained positive and the patient was returned to the Medical Tuberculosis Section on June 3, 1954. At that time, the red-cell count was 5.02 million; hemoglobin, 13.8 Gm.; hematocrit, 44 mm. During the subsequent period of observation, the patient has continued to have an excellent appetite and his mental outlook has been markedly improved.

He has regained approximately 40 pounds in weight. Sputum examinations have remained positive for acid-fast bacilli by concentration and culture. Because of far-advanced bilateral pulmonary tuberculosis, he was not considered a candidate for further surgical therapy.

Comment.—This patient had shown a poor response to therapy until the time of blood volume replacement. He had lost an excessive amount of weight and had been bedfast for approximately one year. Despite a calculated total blood volume deficiency of 993 c.c. and a total hemoglobin mass deficiency of 269 Gm., it was found that 1,000 c.c. of citrated blood and 1,500 c.c. of washed red blood cells were required. Following the total replacement of approximately 375 Gm. of hemoglobin, the laboratory values returned to the normal range and the patient's clinical course was reversed despite the presence of far-advanced active pulmonary tuberculosis.

DISCUSSION

Analysis of the blood volume, plasma volume, and hemoglobin mass deficiencies in this group of 100 cases of pulmonary tuberculosis revealed that 62 per cent of the total group had replaceable hemoglobin deficiencies equivalent to 500 c.c. or more of blood. Sixteen per cent of the total group required one transfusion of 500 c.c. (Fig. 2). In this group, there were no clinical manifestations of the deficiency and this would be of importance only when computing blood replacement requirements at the operating table. Forty-six per cent of the group required the hemoglobin equivalent of 1,000 c.c. or more of blood. These are major blood volume deficiencies and the clinical manifestations of the deficiency are usually present. This figure becomes more significant when interpreted in terms of expected total hemoglobin mass when a 1,000 c.c. deficiency could represent a deficiency of 20 to 30 per cent of the normal value in the individual case. It was surprising to find that 23 per cent of the total group required 1,500 c.c. or more of blood and 8 per cent required 2,000 c.c. or more. It is apparent that despite continuous hospitalization and treatment for pulmonary tuberculosis, the clinical evidence of these deficiencies was mistaken for manifestations of the pulmonary tuberculosis and that the inaccuracy of the red-cell count, hemoglobin, and hematocrit had not been considered. One can only speculate concerning the duration of these deficiencies in blood volume and how the patient's clinical course would have been altered if volumetric blood replacement had been accomplished earlier in the course of the illness. It appears from the frequency of total blood volume deficiencies that this important phase of supportive treatment for a chronic illness had been neglected.

Weight loss alone failed to isolate accurately those cases with a major blood volume deficiency although it was noted that a weight loss of 20 per cent or more of body weight usually reflected a major deficiency. Examination of Tables I and II indicates that 5 patients of the group (A), 38 patients with normal calculated blood volumes, had weight losses of 20 per cent or more which makes it impossible to formulate any absolute rule relative to the weight loss–blood volume relationship.

It appears then that the best method of detecting a major blood volume deficiency is by clinical observation of the patient. The clinical picture is constant and is characterized by anorexia, lack of energy, easy fatigability, lassitude, inability to regain weight losses or maintain a constant weight, and pallor of the facies and conjunctivae. A valuable sign that we have seen with regularity is a collapse of the peripheral superficial veins. Despite the use of a tourniquet, the veins of the arm fail to distend and venepuncture is difficult. These signs and symptoms have been considered to be a manifestation of the chronic pulmonary disease. This is easily disproved because this group of signs and symptoms can be completely eliminated in the majority of cases. Total blood volume and hemoglobin mass replacement is usually followed by a return of appetite which requires an increase in caloric intake, renewed energy, and enthusiasm for life, and a reversal of the weight curve. The listless patient who spends much of his time resting in bed has been observed to become a disciplinary problem because of the additional energy which makes it difficult for him to conform to the usual rest requirements.

A quantitative method for determination of blood volume deficiency must be available. The Evans blue dye method (T-1824) was selected for the basic plasma volume determinations for the following reasons. The method is readily adapted to the average laboratory and gives reproducible results in serial determinations. Reports in the literature comparing the results of T-1824 plasma volume determinations and the I^{131} labeled human serum albumin method indicate that the results obtained by the two methods were not statistically different.[11] The reports of Storaasli and Aust and their coworkers[12, 13] suggest that the plasma volume value obtained by the I^{131} method is lower than by the Evans blue dye method. Blood studies utilizing radioactive Cr^{51} tagged red blood cells are said to yield a blood volume value 16.3 per cent lower than those obtained by the T-1824 method.[14] Since chronic pulmonary tuberculosis presents the problem of a diminished pulmonary reserve and poor tolerance of a vascular overload, the error introduced by the relatively higher value obtained by the T-1824 method and used in the calculation of the deficiency would result in an error which would tend toward undertransfusion rather than vascular overload.

Despite arguments relative to the method utilized to determine plasma and blood volume, the major problem today in the calculation of the individual deficiency is expressed by the question, "What represents this patient's normal expected blood volume?" Rowntree and Brown[15] and Gibson and Evans[16] concluded that the blood volume had a more constant relationship to body surface than to weight. Accumulated data presented by Gregersen[7] and Clark and associates[1] indicate that a close relationship exists between blood volume and body weight and that normal values for blood volume may be calculated safely from observed weight. An analysis of thirty-eight normal blood volume determinations reported here revealed an average blood volume of 81 c.c., plus or minus 9 c.c. per kilogram of body weight with a range of 54 c.c. to 98 c.c. per kilogram and an average plasma volume of 44 c.c., plus

or minus 7 c.c. per kilogram of body weight with a range of 38 c.c. to 55 c.c. per kilogram of body weight. Although the average values of 81 c.c. per kilogram for blood volume and 44 c.c. per kilogram plasma volume agree with average values reported by Gregersen[7] of 85 c.c. and 45 c.c. per kilogram, respectively, and those reported by Clark[1] of 82 c.c. and 45.5 c.c. per kilogram, respectively, it is apparent from the variation of one standard deviation that the correlation with weight is poor. If the values of 85 c.c. per kilogram of body weight for blood volume, and 45 c.c. per kilogram for plasma volume are accepted, it must be realized that the calculated blood and plasma volumes must represent only an approximation of the actual value. This must be considered in volumetric blood replacement and careful control of replacement utilized in order to prevent circulatory overload. The calculation of the normal expected blood volume based upon the normal weight or ideal weight for height, sex, and age represents the greatest source of error in the calculation of blood volume deficiencies.

When the actual deficiency has been calculated and replacement requirements for whole blood and washed red blood cells have been established, a replacement plan must be utilized. It has been our policy to replace one half of the calculated deficiency without hesitation. Transfusions thereafter are given at weekly intervals at the rate of 100 c.c. per hour with careful check of the patient's blood pressure and pulse. In the interval between transfusions, red-cell counts, hemoglobin and hematocrit determinations are obtained. While these values remain within the normal expected limits, blood replacement is continued, but with the first indication of elevated values, replacement therapy is assumed to be completed. Using this system we have had no evidence of circulatory overload.

The final question to be answered then is, "Does the clinical benefit derived from total blood volume replacement offset the inherent dangers of intravenous blood transfusion today?" During the past seven years, transfusions of citrated blood have been given at this hospital with an average reaction rate of 1.65 per cent. These were classified as minor reactions characterized by chills, fever, and urticaria. There was no record of a major hemolytic reaction secondary to the administration of incompatible blood through either laboratory or handling errors. Thompson and Sutliff[17] reported 32 cases of viral hepatitis following blood transfusion from a total of 13,567 transfusions of 500 c.c. citrated blood administered at Kennedy Hospital between 1947 and 1951. Twenty of this group had also received irradiated or nonirradiated plasma. The ratios of viral hepatitis cases to units of infusion reported by those authors were irradiated plasma 1:258, nonirradiated plasma 1:116, and blood 1:424. During the past three years, there have been 2 cases of viral hepatitis following blood transfusion on our service with full recovery in each case. No major hemolytic reactions have occurred. It is felt that the clinical benefits of volumetric blood replacement far exceed the inherent dangers of transfusion.

Numerous authors[1-5] have presented the problem of diminished circulating blood volume in the chronically ill patient and the surgical significance of

reduced blood volume has been stressed by Clark and co-workers.[1] This has been described as chronic shock. It has been demonstrated that restoration of blood volume must precede significant recovery in weight. Holman and associates[4] have demonstrated that when deficiencies of both hemoglobin and tissue protein exist the restoration of protein deficits can be augmented by the correction of the anemia. We have seen this principle demonstrated following blood volume restoration in our patients. In view of the surgical significance of major blood volume deficiency and its effect upon the normal reparative processes in chronic disease, the importance of replacement of blood volume deficits cannot be too strongly emphasized.

SUMMARY

Significant replaceable deficiencies in blood volume, plasma volume and hemoglobin mass have been found in 62 per cent of a survey series of 100 unselected patients with pulmonary tuberculosis presented as candidates for thoracic surgery. Average deficiencies found were 12 per cent in blood volume, 19 per cent in hemoglobin mass, and 8 per cent in plasma volume.

The major deficiency was in hemoglobin mass and exceeded the hemoglobin equivalent of 500 c.c. of whole blood in 62 per cent of the total series; 1,000 c.c. in 46 per cent of the series; 1,500 c.c. of blood in 23 per cent; and 2,000 c.c. in 8 per cent of the entire group.

Blood volume determination is the best method available for evaluating volumetric deficiencies and should be employed in chronic pulmonary tuberculosis in order to provide better supportive therapy in both the medical and surgical phases of treatment.

A discussion of the problems associated with volumetric blood replacement therapy is presented.

REFERENCES

1. Clark, J. H., Nelson, W., Lyons, C., and Mayerson, H. S.: Chronic Shock: The Problem of Reduced Blood Volume in the Chronically Ill Patient, Ann. Surg. **125**: 618-646, 1947.
2. Chang, H. C.: Plasma Protein and Blood Volume, Proc. Soc. Exper. Biol. & Med. **29**: 829-832, 1932.
3. Varco, R. L.: Preoperative Dietary Management for Surgical Patients With Special Reference to Lesions of the Stomach and Duodenum, Surgery **19**: 303-378, 1946.
4. Holman, R. L., Mahoney, E. B., and Whipple, G. H.: Blood Plasma Protein Regeneration Controlled by Diet, Liver and Casein as Potent Diet Factors, J. Exper. Med. **59**: 251-267, 1934.
5. Elman, R., and Davey, H. W.: Studies on Hypo-albuminemia Produced by Protein-deficient Diets: The Correction of Hypoalbuminemia in Dogs by Means of Large Plasma Transfusions, J. Exper. Med. **77**: 1-5, 1943.
6. Hay, E. B., Hay, C. R., and Jenkins, D. E.: Blood Volume and Extracellular Fluid in Tuberculosis, J. THORACIC SURG. **21**: 42-47, 1951.
7. Gregersen, M. I.: Practical Method for Determination of Blood Volume With Dye T-1824, J. Lab. & Clin. Med. **29**: 1266-1286, 1944.
8. Gibson, J. G., Jr., and Evelyn, K. A.: Clinical Studies of Blood Volume; Adaptation of the Method to the Photo-electric Microcolorimeter, J. Clin. Invest. **17**: 153-158, 1938.
9. Abbot, W. E., and Mellors, R. C.: Total Circulating Plasma Proteins in Surgical Patients With Dehydration and Malnutrition, Arch. Surg. **46**: 277-288, 1943.
10. Freinkel, N., Schreiner, G. E., and Athens, J. W.: Simultaneous Distribution of T-1824 and I^{131} Labelled Human Serum Albumin in Man, J. Clin. Invest. **32**: 138-148, 1953.

11. Schultz, A. L., Hammarsten, J. F., Heller, B. I., and Ebert, R. V.: A Critical Comparison of the T-1824 Dye and Iodinated Albumin Methods for Plasma Volume Measurement, J. Clin. Invest. **32:** 107-112, 1953.
12. Storaasli, J. P., Krieger, H., Friedell, H. L., and Holden, W. D.: The Use of Radioactive Iodinated Plasma Protein in the Study of Blood Volume, Surg., Gynec. & Obst. **91:** 458-464, 1950.
13. Aust, J. B., Chou, S. N., Marvin, J. F., Brackney, E. L., and Moore, G. E.: A Rapid Method of Clinical Total Blood Volume Determination Using Radioactive Iodinated Human Serum Albumin (RIHSA), Proc. Soc. Exper. Biol. & Med. **77:** 514-518, 1951.
14. Prentice, T. C., Olney, J. M., Jr., Artz, C. P., and Howard, J. M.: Studies of Blood Volume and Transfusion Therapy in the Korean Battle Casualty, Surg., Gynec. & Obst. **99:** 542-554, 1954.
15. Rowntree, L. G., and Brown, G. E.: The Volume of the Blood and Plasma in Health and Disease, Philadelphia, 1929, W. B. Saunders Company.
16. Gibson, J. G., and Evans, W. A., Jr.: Clinical Studies of Blood Volume: Clinical Application of a Method Employing the Azo Dye "Evans Blue" and the Spectrophotometer, J. Clin. Invest. **16:** 301-316, 1937.
17. Thompson, J. L., Jr., and Sutliff, W. D.: Viral Hepatitis Following the Use of Ultraviolet Irradiated Human Plasma, South. M. J. **45:** 801-805, 1952.

Discussion

DR. LEO ELOESSER, San Francisco, Calif.—It is difficult for me and perhaps for others to follow Dr. Kehne in mathematical considerations involved in these studies. Might I ask him please to explain to us why he selects as a modality the relation of the blood volume to the body surface rather than the body weight; or, indeed, why he selects that modality at all in preference to just an ordinary hemoglobin percentage determination.

DR. KEHNE (Closing).—There are numerous reports in the literature related to the method volumetric expression of blood and plasma volume, and there are some authors who have found that the correlation of blood volume and plasma volume with body weight is best. There are others who maintain that the correlation with body surface, which takes into account both height and weight, gives the best correlation. We have studied about 250 patients and have found that the obesity factor introduces a special problem. In patients weighing 160 pounds or more no correlation could be found between blood volume and weight. It has been suggested that the use of a blood volume-weight correlation based upon the standard weight tables is necessary in the obese patient. In our hands the blood volume-body surface correlation was not entirely satisfactory, but was best in the universal group. The major problem in the calculation of blood volume deficiencies is that it is difficult to establish what constitutes the normal blood volume for a given person unless we have had a preliminary determination in the normal healthy state.

The second question is what advantage the total blood volume method has over the usual laboratory determinations. Slide 2 presents the change we see in the chronically deficient patient. We found an average deficiency of 12 per cent in total blood volume and an 8 per cent deficiency in plasma volume. This implies a changing relationship between the total plasma volume and the total blood volume. Laboratory values for the usual cell counts and hematocrit could be valid only if the plasma volume remained unchanged from the normal state. The failure of the usual laboratory determinations to identify the deficient patient is further demonstrated by the fact that 50 per cent of the deficient patients had normal laboratory values. It has been amply demonstrated in the literature that in the presence of this changing relationship between total blood and plasma volume, the usual laboratory values are invalidated.

VENTILATORY PROBLEMS IN THORACIC ANESTHESIA

A Volume-Cycling Device for Controlled Respiration

Viking Olov Björk, M.D., Carl-Gunnar Engström, M.D., Olle Friberg, M.D., Hans Feychting, M.D., and Alvar Swensson, M.D.
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IN THORACIC surgery the anesthesia offers important physiologic and practical problems, the successful solution of which contributes greatly to the total result of the surgical treatment. The institution of controlled respiration in intrathoracic operations has made these operations safer for the patient. It counteracts paradoxical breathing, mediastinal flutter, and the harmful effect of pendulum air. In addition, the operative procedure is greatly facilitated for the surgeon. In spite of this, the establishment of an adequate gaseous exchange is still a major problem in the anesthesia techniques used hitherto.

PHYSIOLOGIC PRINCIPLES OF VENTILATION AND CIRCULATION

In physiologic conditions, the pCO_2 action on the breathing center automatically maintains an adequate alveolar ventilation. During anesthesia with controlled respiration, this sensitive mechanism for regulation of the ventilation is out of action; the responsibility is taken over by the anesthesiologist.

By the administration of a high oxygen percentage in the gas mixture and in the absence of circulatory shunts, arterial hypoxemia is prevented even if there is serious hypoventilation. This is clearly demonstrated in experiments with diffusion respiration.[1, 2] For the proper elimination of CO_2, on the other hand, an adequate alveolar ventilation is necessary. Hypoventilation will result in a respiratory acidosis; hyperventilation in a respiratory alkalosis. Both these conditions, often difficult to recognize without the help of complicated analysis of the arterial blood, are dangerous to the patient. In both conditions the circulation is impaired. If corrective measures are not undertaken, circulatory collapse may supervene.

The gaseous exchange between the lungs and the blood is a diffusion process through the alveolar-capillary membranes. As the CO_2 is highly diffusible through wet membranes, the arterial pCO_2 is the same as the pCO_2 of the alveolar gas to which blood is exposed during its passage through the lung capillaries. For a given patient with a constant CO_2 production, in absence of circulatory shunts, the arterial pCO_2 is a direct function of the magnitude of the alveolar ventilation. Changes in alveolar ventilation will cause changes in the alveolar and arterial pCO_2, inversely proportional to the magnitude of

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the alveolar ventilation. The amount of free carbonic acid in the plasma varies proportionally to its partial pressure. The acid-base balance in the blood plasma is regulated by the buffer system bicarbonate—free carbonic acid. The relationship between the pH and the content of free carbonic acid and bicarbonate in the plasma is expressed in the Henderson-Hasselbalch equation:[3]

$$pH = pK' + \log \frac{BHCO_3}{H_2CO_3} \quad (pK' = \text{a constant } 6.107 \text{ at } 37^\circ \text{ C.}).$$

The total plasma $CO_2 = BHCO_3 + H_2CO_3$. If the total plasma CO_2 is expressed in volumes per cent and the free carbonic acid in mm. Hg, the formula is written:

$$pH = pK' + \log \frac{CO_2 \text{ Vol. } \% - (0.1316 \cdot a \cdot pCO_2)}{0.1316 \cdot a \cdot pCO_2}$$

(a = the solubility coefficient of CO_2 in plasma = 0.521 at 37° C.).

From this equation it is seen that there is a normal pH (7.38–7.41) when the ratio $\frac{BHCO_3}{H_2CO_3}$ is about 20:1, independent of the absolute values of the numerator and the denominator; and inadequate alveolar ventilation will cause a change in the ratio with displacement of the pH. A respiratory acidosis or alkalosis thus occurs. To a certain extent a compensatory retention or elimination of basic ions available for combining with CO_2 to bicarbonate takes place. This may result in a disturbance in the balance of the electrolytes.

The effect on the circulation of pressure breathing in the closed thorax depends on the mean pressures applied to the airways.[4] The importance of a negative phase in pressure breathing to keep the mean pressure on a low level is widely accepted in order to avoid harmful effect on the circulation.[5, 6] A certain fraction of the intrapulmonary pressure is transmitted to the right auricle and the big central veins with a tendency to decrease the venous pressure gradient and thereby even the venous return and the cardiac output. In the presence of normal circulation, this effect is counteracted by a compensatory increase of the peripheral venous pressure, reconstituting the venous gradient. The ability to reconstitute the venous pressure gradient is dependent on normal functioning vasomotor reflexes and the presence of a normal circulating blood volume. In the open thorax, the effect on the circulation of a negative phase and a low mean pressure may be less. The expiratory resistance imposed by a narrow endotracheal tube may lead to an increase in the functional residual air. This can be overcome if the respirator applies negative pressure during expiration. The resultant prevention of excessive lung expansion is often of practical value to the surgeon.

Based on these physiologic principles of ventilation and circulation a method for controlled respiration in thoracic anesthesia has been worked out.

METHOD

First, it is essential to find out the patient's minute ventilation at rest before the operation. It can be calculated fairly accurately[7] and most comfortably

by use of a ventilatory nomogram.[8] It is even better with a direct measurement, especially in patients with impaired pulmonary function.

Controlled respiration with the obtained values for ventilation is administrated by a respirator designed by Engström in 1951,[9-11] which is adapted for

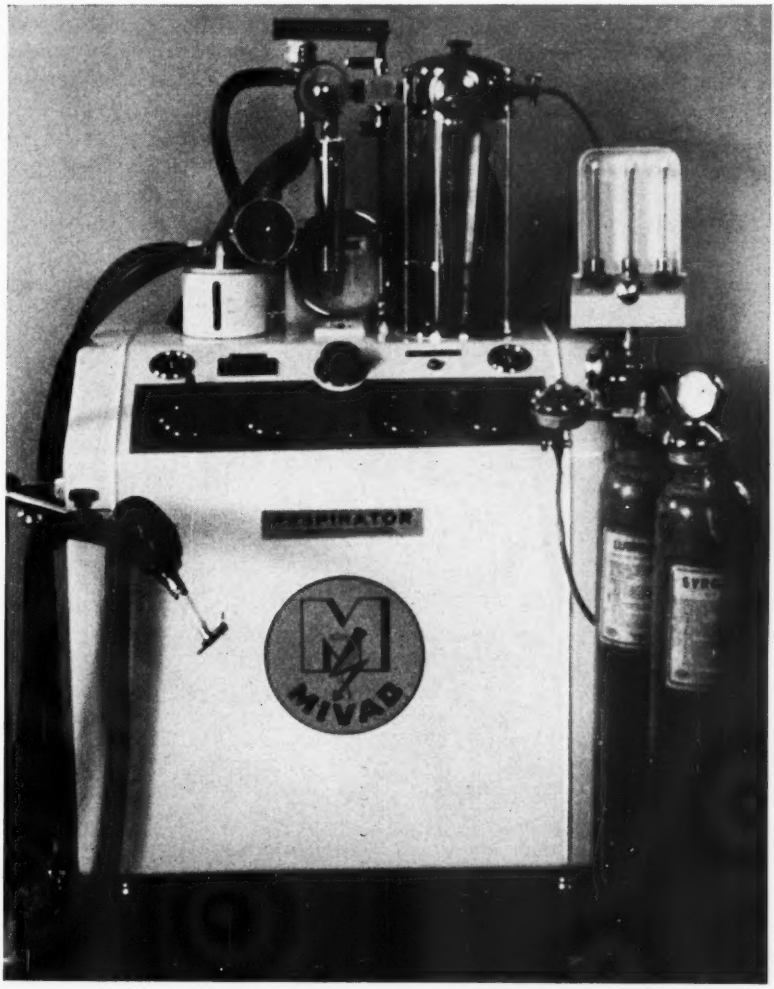
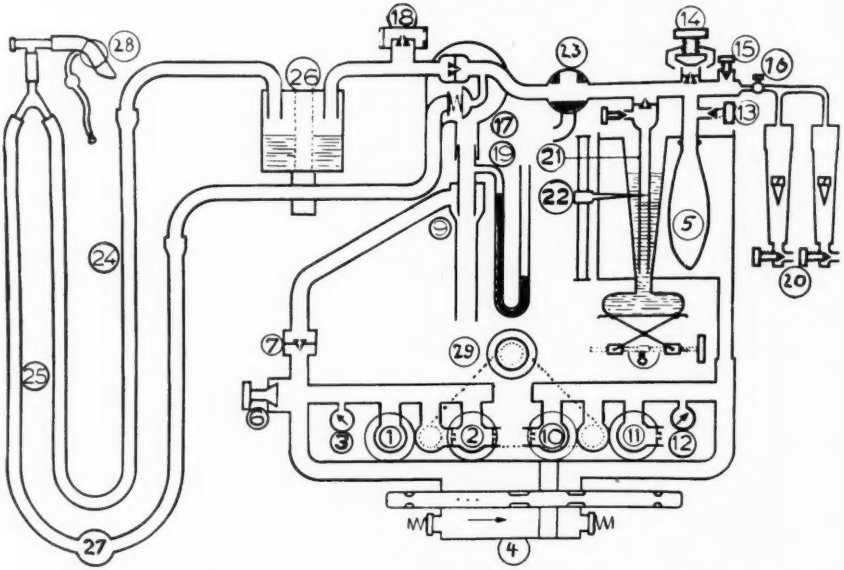


Fig. 1.—*For legend see p. 120.*

giving anesthetics by adding a special rotameter attachment for N_2O and O_2 (Figs. 1 and 2). The gas mixture is insufflated into the air passages *in a semi-open system* (no rebreathing). The respirator is different in principle from the usual types of devices for automatic ventilation during anesthesia. All such

machines in common use are regulated by adjustment of a peak pressure setting and the volume is estimated by the anesthesiologist. This unit, on the other hand, delivers *a pre-set minute volume* at a pre-set respiratory frequency. If the respiratory frequency is changed the pre-set minute volume will not alter. The resultant tidal volume is then calculated from the respiratory frequency and the minute volume. The pressure required to deliver this minute volume will vary from individual to individual; and in the same individual from time to time, since it is determined by the physical characteristics of the lung and chest wall.[12, 13] An increase of the pressure required to force a given volume of gas into the patient's lungs means an alteration of these mechanical factors. *An increased resistance to insufflation will lead to an increased inspiratory pressure and a prolongation of the phase of inspiration.* This will result in a slowing of the rate of gas flow *which will permit the same gas volume to be insufflated with*



Figs. 1 and 2.—The compressor (*4*), which is driven by an electrical A. C. motor, consists of a double cylinder with independent valve systems (*1, 2, 10, 11*) for both pressure chambers. The frequency of the compressor piston is regulated by a stepless mechanical variator (*29*) by which the respiratory frequency can be regulated between 10 and 30 cycles per minute. The pressures from the right part of the compressor are transmitted to a chamber with rigid walls containing a rubber bag. When the piston moves to the left a definite volume of air per time-unit is sucked into the rubber bag (*5*) through an adjustable, calibrated inlet valve (*14*), or the anesthetic gas passes from the rotameters (*20*) into the rubber bag. When the piston moves in the opposite direction the rubber bag is squeezed and the gas insufflated into the air passages of the patient. On the way it passes a waterlock (*21*), a pressure-controlled expiratory valve (*17*), which during the inspiratory phase closes the expiratory passage, and a humidifier (*26*). Before the piston comes to the end of the stroke an automatic pressure release on the piston shaft is opened, which causes a rapid drop in pressure. When the pressures squeezing the rubber bag are set to a higher value than the pressure fluctuation on the manometer in the waterlock the rubber bag will be deflated before the piston comes to the end of the stroke. Thus, there will exist a pressure "reserve" around the outside of the rubber bag, which will be used to overcome any increased resistance in the patient's circuit. The left part of the compressor cylinder supplies the positive pressure fluctuations for operation of the ventury (*9*) which in turn applies an intermittent negative pressure on the atmospheric side of the expiratory valve. This is transmitted to the airway and empties the patient's lungs.

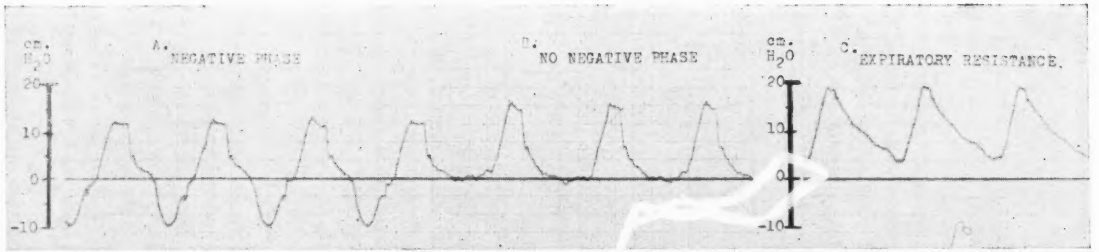


Fig. 3.—Pressure pattern produced by the described device in a narcotized and curarized patient with pulmonary tuberculosis (undergoing lobectomy). The pressures are recorded in the upper part of trachea by closed thorax. Minute ventilation of 9 L. per minute and respiratory frequency of 22 cycles per minute are the same in all tracings.

A, A negative phase of −10 cm. H_2O is applied. Mean pressure = +1 cm. H_2O. *B*, Only positive pressure phase. Note increase of the maximal intratracheal pressure. Mean pressure = +4.3 cm. H_2O. *C*, An expiratory resistance is added. Further increase of the maximal intratracheal pressure. Mean pressure = +9.9 cm. H_2O.

a comparatively smaller pressure increase. This automatic pressure adjustment and adjustment of the rate of gas flow is most important for the successful management of prolonged artificial ventilation in patients with unfavorable factors for the ventilation. The development of dangerous pressures is prevented by a water level safety valve system. Similarly, the negative pressure applied during exsufflation can be regulated. Thus, the mean mask pressure can be kept at a low level (in normal lungs down to zero pressure). By application of a regulating expiratory resistance, it is also possible to operate with high mean mask pressure and with the lungs in expanded position. In spite of this, the patient will get the same amount of ventilation until the safety pressure is reached and gas escapes through the waterlock. Thus, *the mean mask pressure and hereby even the level of the functional residual air can be closely controlled in the presence of a constant minute volume* (Fig. 3). The expiratory volume can be measured to control leakage, if any. The composition of the gas mixture to the patient is exactly known.

COMMENT

Empirically, it is impossible to estimate whether or not the ventilation to a patient under anesthesia is adequate. Several authors have reported severe disturbances in the acid-base balance during thoracic anesthesia.[14-18] As methods for controlling the ventilation by measuring the gas tensions in the arterial blood or alveolar gas are not convenient for practical use, the best method is to control the ventilatory volumes which may serve as a satisfactory index of the adequacy of ventilation.

Different systems may allow volume-recording apparatus (spirometers, pneumotachographs) to be built in. In systems so far used which are pressure controlled, the minute volume will alter according to the alterations in the mechanical factors of the pulmonary ventilation. By use of the described volume-cycling device the patient receives a predetermined ventilartory volume satisfactorily corresponding to his requirements. This is maintained during the operation in spite of variations in the mechanical factors caused by pressure on the lung, traction on the bronchi, and so on.

The described method for controlled respiration has been used in about 70 major intrathoracic interventions in patients most of whom had impaired pulmonary function. By this method it has been possible in 1 patient to keep his ventilation adequate during operation on the only remaining lung. Segmental resection of the left upper lobe was performed. In another patient, both upper lobes were removed in the same stage. Even in "bad risk" patients, the blood pressure and pulse rate have remained remarkably steady during operations lasting for as long as nine hours, indicating that a good circulation has been maintained.

It is often stated that patients in poor condition should receive the highest possible concentration of oxygen in the inspired atmosphere during the operation. Potent anesthetic agents, which allow an oxygen percentage of 80, 90, even 95 per cent, are often advocated. It may be questioned whether this attitude is quite correct. In our opinion, it is preferable to ensure ade-

quate ventilation with sufficient but not excessive oxygen concentration, since then the possibility of hypercapnia will be avoided. Our results in poor-risk patients with N_2O as the anesthetic agent seem to justify such an opinion.

In cases with respiratory insufficiency during the immediate postoperative period after pulmonary resections, the same device is successfully used for artificial respiration.[12]

SUMMARY

For the administration of controlled respiration, a volume-cycling positive-negative pressure device (the Engström Respirator) has been used on a series of about 70 patients undergoing major intrathoracic operations. The method has proved most valuable and offers in the main the following advantages:

1. Dangerous hypo- and hyperventilation is prevented by the administration of a determined ventilatory volume, maintained independently of altered mechanical conditions, such as opening of the pleura, compression of the lung, and traction on the bronchus.

2. Respiration with a negative expiratory phase and low mean pressure favors the circulation, and makes it possible to ventilate the patient when only narrow endotracheal tubes can be used. The degree of expansion of the lungs can be controlled with maintenance of a constant minute volume, and this often facilitates the work of the surgeon.

3. The composition of the gas mixture administered to the patient is exactly known.

REFERENCES

1. Draper, W. B., Whitehead, R. W., and Spencer, J. N.: Studies on Diffusion Respiration; Alveolar Gases and Venous Blood pH of Dogs During Diffusion Respiration, Anesthesiology **8**: 524, 1947.
2. Lechtenbörger, H., Valentin, H., Venrath, H., Fruhmann, G., özsoy, I. S., Steinforth, H., Schmitz, Th., and Griesemann, H.: Der Gasstoffwechsel bei akutem Atemstillstand, Thoraxchirurgie **2**: 250, 1954.
3. Peters, J. P., and Van Slyke, D. D.: Quantitative Clinical Chemistry I., Baltimore, 1932, Williams & Wilkins.
4. Werkö, L.: The Influence of Positive Pressure Breathing on the Circulation in Man, Acta med. scandinav. supp. **193**: 1, 1947.
5. Maloney, J. V., Jr., Elam, J. O., Handford, S. W., Balla, G. A., Eastwood, D. W., and Ten Pas, R. H.: Importance of the Negative Pressure Phase in Mechanical Breathing Machines, Federation Proc. **11**: 100, 1952.
6. Maloney, J. V., Jr., Affeldt, J. E., Sarnoff, S. J., and Whittenberger, J. L.: Electrophrenic Respiration. IX. Comparison of Effects of Positive Pressure Breathing and Electrophrenic Respiration on the Circulation During Hemorrhagic Shock and Barbiturate Poisoning, Surg., Gynec. & Obst. **92**: 672, 1952.
7. Bühlmann, A., and Luchsinger, P.: Atemphysiologische Bemerkungen zur künstlichen Atmung bei der Behandlung des Tetanus, Helvet. paediat. acta **9**: 403, 1954.
8. Radford, E. P., Jr.: Ventilation Standards for Use in Artificial Respiration, J. Appl. Physiol. **7**: 451, 1955.
9. Sjöberg, A., Engström, C.-G., and Svanborg, N.: Diagnostiska och kliniska rön vid behandling av bulbospinal poliomyelit, Nord. med. **47**: 536, 1952.
10. Engström, C.-G.: Respirator enligt ny princip, Svenska läkartin **50**: 545, 1953.
11. Engström, C.-G.: Treatment of Severe Cases of Respiratory Paralysis by the Engström Universal Respirator, Brit. M. J. **2**: 666, 1954.
12. Björk, V. O., and Engström, C.-G.: The Treatment of Ventilatory Insufficiency After Pulmonary Resection With Tracheostomy and Prolonged Artificial Ventilation, J. THORACIC SURG. **30**: 356, 1955.
13. Christie, R. V.: Dyspnoea in Relation to the Visco-Elastic Properties of the Lung, Proceed. R. S. Medicine **46**: 381, 1953.

14. Beecher, H. K., and Murphy, A. J.: Acidosis During Thoracic Surgery, J. THORACIC SURG. **19**: 50, 1950.
15. Taylor, F. H., and Roos, A.: Disturbances in Acid-Base Balance During Ether Anesthesia, With Special Reference to Changes Occurring During Thoracic Surgery, J. THORACIC SURG. **20**: 289, 1950.
16. Maloney, J. V., Jr., Derrick, W. S., and Whittenberger, J. L.: A Device Producing Regulated Assisted Respiration. II. The Prevention of Hypoventilation and Mediastinal Motion During Intrathoracic Surgery, Anesthesiology **13**: 22, 1952.
17. Bühlmann, A., and Hotz, M.: Lungenfunktion und Narkose, Helvet. med. acta **18**: 532, 1951.
18. Cara, M.: Inefficacité et danger de l'oxygènothérapie: nécessité de la ventilation le traitement des insuffisances respiratoires, Anesth. et analg. **11**: 421, 1954.

Announcement

New Regulations of the Board of Thoracic Surgery

At a meeting of representatives of the Board of Thoracic Surgery with the American Board of Surgery held on April 26, 1955, in Philadelphia, it was agreed that candidates examined by the American Board of Surgery in Part I (written examination) on or after October 26, 1955, who are certified by the American Board of Surgery, would be required to take only the oral examination given by the Board of Thoracic Surgery.

Before taking the oral examination of the Board of Thoracic Surgery the candidate must furnish satisfactory evidence of having completed three years of training in general surgery and two years of training in thoracic surgery in an approved institution, and that he is a diplomate of the American Board of Surgery.

Candidates examined by the American Board of Surgery in Part I prior to October 26, 1955, will be required to take Part I (written examination) of the Board of Thoracic Surgery before taking its oral examination.